Final Study Report

Study I4V-MC-B025

Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant (baricitinib), a JAK1/2 Inhibitor

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Document ID: VV-PVG-120113

Post Authorisation Safety Study Information

Title:	Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant® (baricitinib) a JAK1/2 inhibitor
Study Identifier	I4V-MC-B025
Version identifier of the final study report	1.0
Date of last version of the final study report	Not applicable
European Union (EU) Post Authorisation Study (PAS) Register Number	EUPAS43239
Active substance	Baricitinib Anatomical Therapeutic Chemical Code: L04AA37
Medicinal product(s)	Baricitinib
Product reference	EMEA/H/C/004085
Procedure number	
Marketing authorisation holder(s)	Eli Lilly Nederland B.V. (Lilly) Papendorpseweg 83 3528 BJ Utrecht The Netherlands
Joint Post Authorisation Safety Study (PASS)	Not applicable
Research question and objectives	This study assessed: 1. The effectiveness of the updated baricitinib healthcare professional Educational Materials and Patient Alert Card among dermatologists and rheumatologists 2. The effectiveness of a Direct Healthcare Professional Communication distributed to dermatologists and rheumatologists
Countries of study	Sweden, France, Germany, and Spain
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1. Abstract

Title: Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant (baricitinib) a JAK1/2 inhibitor.

Keywords: baricitinib, JAK1/2 inhibitor, risk minimisation, rheumatoid arthritis, atopic dermatitis

Rationale and background: Baricitinib is a Janus kinase (JAK) 1/JAK2 inhibitor that was first approved for the treatment of rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs. When baricitinib was first authorised for use in the European Union (EU) in February 2017, additional risk minimisation activities were included as part of the EU Risk Management Plan (RMP).

These activities included:

(i) the Healthcare Professional (HCP) Educational Materials to inform the initial discussion between the rheumatologist and patient at time of first prescribing about important safety information related to the use of baricitinib during pregnancy or breastfeeding, the potential risk of infection, and changes in lipid parameters associated with the administration of baricitinib, and

(ii) a Patient Alert Card (PAC) with the same important safety information described above.

Eli Lilly and Company (Lilly) committed to conduct a survey of rheumatologists to assess the effectiveness of the above listed risk minimisation activities (Study I4V-MC-B010, 2020). The survey was designed to assess rheumatologists' understanding of the important safety information detailed in the HCP Education Materials and assess the communication of the important safety information and distribution of the PAC to patients prescribed baricitinib for the first time.

Subsequently, baricitinib has been approved for the indication of moderate to severe atopic dermatitis (AD) in adult patients who are candidates for systemic therapy and for the treatment of severe alopecia areata (AA) in adult patients.

Additionally, the HCP Educational Materials and the PAC for all indications have been updated to include important safety information on venous thromboembolism (VTE), major adverse cardiovascular events (MACE), lymphoma and other malignancies and dosing recommendations.

Also, a Direct Healthcare Professional Communication (DHPC) has been distributed to dermatologists and rheumatologists to draw attention to the increased incidence of MACE, serious infections, VTE and mortality seen with JAK inhibitor treatment.

Research question and objectives: This study assessed the following:

1. The effectiveness of the updated baricitinib HCP Educational Materials and PAC among dermatologists and rheumatologists
2. The effectiveness of a DHPC distributed to dermatologists and rheumatologists

Study design: This study used a multi-national, observational cross-sectional design.

Setting: Eligible dermatologists and rheumatologists from at least 4 EU countries (Sweden, France, Germany and Spain) were invited.

The survey was distributed within 3 months after both the DHPC and updated risk minimisation materials had been distributed in each participating country and Committee for Medicinal Products for Human Use (CHMP) approval of this protocol had been obtained.

The HCP Educational Materials, the PAC and the DHPC were sent to HCPs who were prescribers or potential prescribers of baricitinib in each country, as agreed by each National Competent Authority (NCA).

The target population in each selected country was dermatologists and rheumatologists who had been sent the HCP Educational Materials, the PAC, and the DHPC.

Respondents were invited to complete the survey via the internet. When technical difficulties were encountered, a paper-based survey could be requested.

Subjects and study size, including dropouts:

The study targeted completion of approximately 400 surveys (approximately 200 dermatologists and approximately 200 rheumatologists), with at least 50% of those from dermatologists who had prescribed baricitinib and 50% from rheumatologists who had prescribed baricitinib. This provided an estimated precision of ±7% around the observed proportion of correct responses (for each specialty) who answer correctly, assuming the true proportion was 50%. If the true proportion was greater or lesser than 50%, the estimated proportion would be more precise. The maximum number of completed surveys from any individual country was set to 80 dermatologists and 80 rheumatologists.

Variables and data sources: The survey collected responses to each question required to address the study objectives, in addition to prescriber status (yes/no), demographic information (e.g., country of practice), and clinical experience (e.g., duration of experience treating patients with relevant indication, number of patients for whom they had prescribed baricitinib).

Structured, self-administered surveys comprising closed-ended questions or statements with multiple-choice responses were used to collect the data.

Study Endpoints: For Objective 1, the study endpoints were the correct understanding of each Key Risk Message (KRM) (Questions 8-16 pertaining to pregnancy, lipid changes, infections and VTE, MACE, lymphoma and other malignancies, and dosing as communicated in the HCP Educational Materials).

The survey also assessed whether HCPs (a) communicate important safety information and mitigating actions to patients prescribed baricitinib for the first time, and (b) distribute the PAC to patients prescribed baricitinib for the first time.

For Objective 2, the study endpoints were the correct understanding of the KRM (Questions 17-19) pertaining to the JAK inhibitor class effects communicated in the DHPC.

Data Analysis: Data collected from the survey were reported using descriptive statistics. In addition to the overall analysis of the survey data collected, data were analysed by country, by specialty (dermatologist or rheumatologist) and prescriber status (had previously prescribed baricitinib [i.e., prescriber], had not previously prescribed baricitinib [i.e., potential prescriber]), by number of patients treated, and by clinical experience. Responses to each question relating to the understanding of risks were categorised as "Correct" or "Incorrect." Frequency distributions with 95% confidence intervals (CIs) were calculated for responses to questions that addressed the survey objective (excluding demographic questions).

Results:

A total of 530 HCPs contributed to the main analysis, this included 282 dermatologists and 248 rheumatologists. Many (83.4%) of the HCPs had previously prescribed baricitinib; half (50.5%) of which had treated 1 to 5 patients with baricitinib in the previous 6 months and 46.4% treated 6 or more patients in the last 6 months.

Objective 1

The first objective of this observational study was to assess the effectiveness of the updated baricitinib HCP Educational Materials and PAC among dermatologists and rheumatologists. The KRMs within these materials included those pertaining to:

- KRM#1: Pregnancy (Q8)
- KRM#2: Lipid parameters (Q9)
- KRM#3: Infections (Q10, Q11, Q12)
- KRM#4: VTE (Q13a, Q13b, and Q13c).
- KRM#5: MACE (Q14a, Q14b, and Q14c)
- KRM#6: Lymphoma and other Malignancies (Q15a, Q15b).
- KRM#7: Dosing (Q16a, Q16b, and Q16c).

Response to individual questions

With the exception of one question pertaining to Objective 1, all were answered correctly by at least 71% of rheumatologists/dermatologists who completed the survey.

Individual questions (Q9, Q10, Q11) and items of questions (all 3 items of Question 13; 1 of 3 items of Question 14; 1 of 2 items of Question 15; and 2 of 3 items of Question 16) all had responses greater than 80%.

The only question for which the response was less than 71% was for Question 14b, where only 66.8% of respondents correctly identified that the statement, "Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors," was false. This result should be put into context with the other two questions on the cardiovascular risk topic where 91.5% correctly identified that there is a potential increased risk of MACE in patients with certain risk factors using JAK inhibitor treatment including baricitinib and 77.2% correctly identified that in patients who are past or current smokers, baricitinib should only be used if no suitable alternatives are available.

Responses to key risk messages

To be counted as demonstrating understanding of a specific KRM, respondents were required to answer all questions/items of the KRM correctly. Respondents' demonstrated understanding of the risk messages pertaining to Objective 1 were as follows:

- KRM#1 Pregnancy (Q8), 73.0%
- KRM#2 Lipid parameters (Q9), 90.4%
- KRM#3 Infections (Q10, Q11, Q12), 73.4%
- KRM#4 VTE (Q13a-c), 81.9%
- KRM#5 MACE (Q14a-c), 47.9%
- KRM#6 Lymphoma and other malignancies (Q15a-b), 66.0%, and
- KRM#7 Dosing (Q16a-c), 52.8%

Objective 2

The second objective of this observational study was to assess the effectiveness of a DHPC distributed to rheumatologists and dermatologists. The development of the DHPC was at the request of the Pharmacovigilance and Risk Assessment Committee following an Article 20 referral. The letter was developed jointly by the 4 EU MAHs of the 5 EU-approved JAK inhibitors and was not specific to baricitinib.

The relevant questions to address Objective 2 were based on 1 KRM regarding the JAK inhibitor class effects (Q17a, Q17b, Q17c, Q17d, Q18, Q19).

For objective 2, more than 80% of respondents answered correctly to Question 17a and 17b which required an answer of true to the question as to whether there was an increased incidence of MACE and VTE observed with JAK inhibitor treatment compared to tumour necrosis factor alpha (TNFα) inhibitors. 78.3% responded correctly that periodic skin examination is recommended for patients treated with baricitinib. This suggests that there is a good understanding of the cardiovascular and thromboembolic risks associated with JAK inhibitors and a good understanding of the recommended medical practice to assess the patient for skin cancer.

For objective 2, there was a much lower percentage of correct responses for questions comparing JAK inhibitors with TNFα inhibitors with respect to serious infections (29.2%), mortality (18.5%) and malignancy (60.6%). A possible explanation for this is that these events are also associated with TNFα inhibitor treatment and respondents may not have known whether the incidence was higher or lower for JAK inhibitors.

Awareness of Additional Risk Minimisation Measure (aRMM) and Communication of Important Safety Information

In addition to the questions pertaining to the HCPs knowledge of risks, the survey included questions to understand awareness of the aRMM and behaviours around communicating risks.

- HCP Educational Material awareness: Slightly more than half of all respondents (52.1%) indicated they were aware of the HCP educational materials. Of these 60.9% reported that they had received a copy of the materials. Of those that reported to have received a copy, 75.6% reported that they had read the materials.
- PAC awareness: Similarly, 52.3% indicated they were aware of the PAC for baricitinib. Of these 8.5% indicated that when prescribing baricitinib for the first time their patient is provided with a PAC. Among 190 respondents who indicated they had both prescribed baricitinib and were previously unaware of the PAC (thus could not have provided it at first prescription), 92.6% indicated that someone in their practice/hospital communicates the important information to their patients when prescribing baricitinib for the first time.
- DHPC letter awareness: About 2/3 of respondents (69.1%) indicated they had received a copy of the DHPC. Of those who reported to have received it, 88.8% respondents indicated that they had read it.

The high level of knowledge of the safety information in the KRM demonstrated in Objective 1 results, combined with the relatively low number of respondents who were aware of and read the aRMM, suggests that either the respondents did not recall accurately the receipt of the materials or that HCPs obtained safety information from other sources in addition to the HCP Educational Materials.

It is worth noting that the PACs are also distributed directly to the patient, as they are attached to the PIL which is provided with every package of baricitinib.

Discussion:

The present study achieved its key objectives through the successful attainment of its target sample size and recruitment of participants who were diverse with respect to their geographic region, duration of practice within their specialty, and experience with the treatment of patients with baricitinib.

Overall results indicate that 14.3% and 7.5% of HCPs demonstrated an understanding of all KRMs that constituted the first and second objective, respectively. While these appear to be relatively small percentages, these figures represent those who answered all questions associated with each KRM correctly. Therefore, further consideration of individual questions that comprise

each KRM is instructive and can aid in contextualising these more restrictive estimates. From this perspective, 15 of the 16 questions that constituted the KRMs of objective 1 are above 71%. These results were aligned with a prior non-interventional PASS study (I4V-MC-B010, 2020), which assessed understanding of the educational materials related to pregnancy and breastfeeding, infections, reactivation of viral infections and changes in lipid parameters. Additionally, 3 of the 6 questions constituting KRM #8 of Objective 2 were above 78%.

While this study is descriptive and there were no pre-specified criteria for demonstrating effectiveness of aRMM, the results suggest that practicing dermatologists and rheumatologists are largely aware of the communicated risks of baricitinib.

This HCP survey took place across four EU countries where baricitinib is marketed for the indications of RA, AD, and AA. In order to ensure there was equal spread across the four countries and to maximise generalisability, a limit of a maximum of 80 surveys for each speciality in each country was made. Recruitment into the survey was rapid and as a result, more than 80 surveys from dermatologists in Germany were obtained. Whilst the primary analysis included only the first 80 German dermatologists, a post-hoc analysis including all the responses from the 81st to the 131st dermatology respondents in Germany indicated there was no change in understanding each of the KRMs.

Overall, 76.4% of respondents were prescribers of baricitinib indicating that the survey was representative of prescribers.

Participants were self-selected since they voluntarily responded to the invitation to participate, so the potential exists that those who choose to respond to the survey may differ in their understanding of the important safety information from those who elect not to participate. All data from the survey were self-reported and therefore susceptible to possible reporting bias in that respondents may select the socially desirable response rather than the true response. This may be particularly true for the questions regarding the receipt and reading of the DHPC.

Conclusion:

The results of this survey showed that:

- 15 of the 16 individual questions pertaining to KRMs of baricitinib were correctly answered by at least 71% of HCPs:
    - Understanding was highest for the overall risk messages around need to monitor lipids and risk of VTE. Understanding was lowest for risk messages around risk of MACE and dosing.
- Subgroup analyses according to specialty were generally consistent with slightly better understanding of safety messages among rheumatologists than dermatologists.
- Awareness of the specific aRMM (i.e., the HCP Education Material and the PAC) was modest with 52% of HCPs aware of each. Despite low awareness of the HCP Educational Material, knowledge of risks was high. Despite low awareness of the PAC, 92.6% of

HCPs that are unaware of the PAC and prescribe baricitinib communicate risk information at first prescription.

- 69.1% of respondents indicated they received a copy of the DHPC, and 88.8% of those respondents indicated reading it. Given that the distribution of the DHPC is complete, risk messages for baricitinib are understood based on Objective 1, and consistent with Good Pharmacovigilance Practices Module XVI Rev 3, the DHPC can be removed from the baricitinib EU RMP as an aRMM activity.

The results of this study support that both rheumatologists and dermatologists have good understanding of the risks associated with baricitinib. This is consistent with a previous survey assessment of baricitinib aRMM effectiveness for rheumatologists (I4V-MC-B010, 2020) and for the first time provides evidence that dermatologists also understand the safety information for baricitinib. This understanding of risks is likely resulting from a combination of risk minimisation activities including routine (Summary of Product Characteristics) and additional activities (such as the aRMM).

Based upon this current evaluation of the knowledge, understanding and behaviours, the aRMM were determined effective. No changes to the ongoing aRMM are warranted based on the results of this study.

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2. List of Abbreviations

Term	Definition
aDCT	Annotated Data Collection Tool
AA	alopecia areata
AD	atopic dermatitis
aRMM	additional risk minimisation measure
B025	Study I4V-MC-B025
CHMP	Committee for Medicinal Products for Human Use
CI	confidence interval
DHPC	Direct Healthcare Professional Communication
EDC	electronic data capture
EMA	European Medicines Agency
EU	European Union
GDPR	General Data Protection Regulation
GVP	Good Pharmacovigilance Practices
HCP	healthcare professional
HMA	Head of Medicines Agency
IT	Information Technology
JAK	Janus kinase
KRM	Key Risk Message
Lilly	Eli Lilly and Company
MACE	major adverse cardiovascular event
MAH	Marketing Authorisation Holder
N/A	not applicable
NCA	National Competent Authority
PAC	Patient Alert Card
PAS	post authorisation study
PASS	post authorisation safety study
PRAC	Pharmacovigilance and Risk Assessment Committee
RA	rheumatoid arthritis
RMM	risk minimisation measures
RMP	Risk Management Plan
SAS	Statistical Analysis Software

Term	Definition
SDLC	System Development Life Cycle
SOPs	Standard Operating Procedures
SCC	Survey Coordinating Centre
TNFα	Tumour Necrosis Factor alpha
UBC	United BioSource LLC
UK	United Kingdom
USA	United States of America
VTE	venous thromboembolism

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4. Other Responsible Parties

None

5. Milestones

Milestone	Planned date	Actual date
Submission of protocol	25 April 2023	24 April 2023
Start of data collection	Estimated by 31 October 2023[a]	31 March 2024
End of data collection	Estimated at 31 October 2024	31 October 2024
Registration in the HMA-EMA Catalogue of real-world data sources and studies	Prior to start of data collection	04 October 2021[b]
Final report of study results	30 April 2025	See date on Page 1

Abbreviations: CHMP = Committee for Medicinal Products for Human Use; DHPC = Direct Healthcare Professional Communication; EMA = European Medicines Agency; HCP = healthcare professional/provider; HMA = Heads of Medicines Agencies; PAC = Patient Alert Card.

[a] The proposed start date for the survey was dependent on the timing of the CHMP opinion of the protocol (based on EMA timetable for Post Authorisation Measure assessment) as well as the DHPC distribution and implementation of updated risk minimisation materials (i.e., the PAC and HCP educational materials) in each participating country. CHMP opinion on protocol was achieved on 14 December 2023.

[b] Study was first registered in October 2021; protocol was uploaded 21 May 2024.

6. Rationale and Background

Baricitinib is a Janus kinase (JAK) 1/JAK2 inhibitor that was first approved for the treatment of rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs. When baricitinib was first authorised for use in the European Union (EU) in February 2017, additional risk minimisation activities were included as part of the EU Risk Management Plan (RMP).

These activities included:

(i) the Healthcare Professional (HCP) Educational Materials to inform the initial discussion between the rheumatologist and patient at time of first prescribing about important safety information related to the use of baricitinib during pregnancy or breastfeeding, the potential risk of infection, and changes in lipid parameters associated with the administration of baricitinib, and

(ii) a Patient Alert Card (PAC) with the same important safety information described above.

Eli Lilly and Company (Lilly) previously conducted a survey of rheumatologists to assess the effectiveness of the above listed risk minimisation activities (Study I4V-MC-B010, 2020). The survey was designed to assess rheumatologists' understanding of the important safety information detailed in the HCP education materials and assess the communication of the important safety information and distribution of the PAC to patients prescribed baricitinib for the first time. The final study report for Study B010 concluded that the risk minimisation materials were effective; rheumatologists understood the safety information for baricitinib and communicated these messages to their patients (Procedure EMEA/H/C/004085/II/0017 with Committee for Medicinal Products for Human Use [CHMP] positive opinion 29 October 2020).

Subsequently, baricitinib was approved for the indication of moderate to severe atopic dermatitis (AD) in adult patients who are candidates for systemic therapy in October 2020 and for the treatment of severe alopecia areata (AA) in adult patients in June 2022. With the expansion of marketing authorisation into dermatologic conditions, Lilly originally committed to survey dermatologists to ensure the risk minimisation materials were also effective among dermatologists (Study I4V-MC-B025; committed to in EU RMP v8.1 [Procedure EMEA/H/C/004085/II/0016]).

Implementation of Study B025 was paused as part of a safety variation submitted to the Pharmacovigilance and Risk Assessment Committee (PRAC) by Lilly 29 October 2021, and then by the Article 20 referral for JAK inhibitors (10 February 2022). With the completion of the Article 20 referral (10 March 2023), the scope of B025 was expanded to include rheumatologists as well as dermatologists, and to assess the resulting Risk Minimisation Measures (RMMs) which included updated educational materials and a Direct Healthcare Professional Communication (DHPC). The HCP Educational Materials and the PAC for all indications were updated to include additional important safety information on venous thromboembolism (VTE),

major adverse cardiovascular events (MACE), lymphoma and other malignancies and dosing recommendations.

The DHPC was distributed to dermatologists and rheumatologists to communicate the increased incidence of MACE, serious infections, VTE and mortality seen with JAK inhibition treatment compared to tumour necrosis factor inhibitors.

7. Research Question and Objectives

Research Questions and Objectives: This study assessed the following:

1. The effectiveness of the updated baricitinib HCP Educational Materials and PAC among dermatologists and rheumatologists. The key risk messages (KRMs) within these materials included those pertaining to:
    a. Pregnancy
    b. Infections
    c. Changes in lipid parameters
    d. VTE
    e. MACE
    f. Lymphoma and other malignancies
    g. Appropriate dosing
2. The effectiveness of a DHPC distributed to dermatologists and rheumatologists.

8. Amendments and Updates

Not applicable.

9. Research Methods

9.1. Study Design

This observational study was a multi-national cross-sectional survey.

Descriptions of the study research methods herein are based on the Protocol Amendment (c), dated 01 March 2024 (Appendix 1.1).

9.2. Setting

Eligible dermatologists and rheumatologists from 4 EU countries (Sweden, France, Germany, Spain) were invited. These countries were chosen based upon sufficient market uptake of baricitinib to support target enrolment and sufficient numbers of dermatologists and rheumatologists who had indicated they were willing to participate in this type of research.

The survey was distributed in Sweden, France and Germany within 3 months after both the DHPC and updated risk minimisation materials were distributed in each participating country and approval of this protocol had been obtained. The survey was distributed later in Spain to reach target sample size for the respondents.

To maximise the generalisability of the survey results, the protocol indicated a maximum number of completed surveys that were to be accepted from each country, so that no individual country was over-represented. No more than 80 completed surveys from each speciality were accepted from any one country, i.e., a maximum of 80 dermatologists from each country and 80 rheumatologists from each country. If the target enrolment had not been met, additional EU countries would have been considered. This is consistent with the addition of Spain to the survey. The HCP Educational Materials, the PAC and the DHPC were sent to HCPs who were prescribers or potential prescribers of baricitinib in each country, as agreed by each National Competent Authority (NCA). Of note, an error in the survey execution resulted in more than 80 respondents being allowed in one country for one speciality. See Section 9.9.1 and Section 9.9.5 for more details and how the analysis was handled for this error.

The target population in each selected country were dermatologists and rheumatologists who were sent the HCP Educational Materials, the PAC and the DHPC.

The same survey was used for all participating countries to ensure consistency in testing the target population. As such, variability of survey results based on geography was not anticipated.

The questions and statements included in the survey were constructed to test the understanding of the goals of the additional risk minimisation measures (aRMMs). Completed surveys were analysed to determine a correct response rate for each question related to the main objectives of the study.

Respondents were able to complete the survey via the internet. This allowed respondents to participate at a time and location that was convenient for them. If a survey had been started by the HCP but could not be completed due to any technical issues, the HCP could contact the Survey Coordinating Centre (SCC) for a paper survey to complete.

9.3. Survey Target Population

The target populations for the survey were dermatologists and rheumatologists in the EU who had previously self-identified as being willing to receive invitations for survey research. The survey launched in Sweden, France, and Germany on 31 March 2024 and the survey in Spain launched on 07 October 2024.

9.3.1. Inclusion Criteria

Dermatologists or rheumatologists met the following criterion for inclusion in the survey:

- Must identify themselves as being previous prescribers or potential prescribers of baricitinib.

To ensure that survey results adequately reflect the knowledge of the main target population of the survey; at least 50% of the total completed surveys for each speciality were required from prescribers of baricitinib.

9.3.2. Exclusion Criteria

Dermatologists or rheumatologists meeting the following criterion were not permitted to take the survey:

- Current or past employment with Lilly or any of its affiliates, United BioSource LLC (UBC), IQVIA, the European Medicines Agency (EMA) or any NCA.

9.4. Variables

The survey contained a total of 27 questions (Q) relating to: eligibility (Q1-3, Q6), description of eligible respondents (Q4-7), understanding of safety information (Q8-19), awareness and behaviours pertaining to HCP Educational Materials (Q20-22), awareness and behaviours pertaining to the PAC (Q23, Q25), and communication of the important safety information (Q24, Q26-27). The survey is provided in Annex 1, Appendix 1.1 of the protocol [Annex 1, Appendix 1.1 of this document].

These survey questions provided the variables needed to address the 2 study objectives:

Objective 1:

- Response to questions about important safety information detailed in the HCP Educational Material (Q8-Q22). The analysis and arrangement of the individual safety questions into “key risk messages” is detailed further in Section 9.9.2.
- Whether or not important safety information and related risk mitigation actions were communicated to patients prescribed baricitinib for the first time (Q24, and Q6 to assess whether they prescribe baricitinib), and
- Whether the PAC was distributed to patients prescribed baricitinib for the first time (Q25, along with Q6 and Q23 to assess whether they were aware of the PAC).

Objective 2:

- Responses to questions about important safety events observed with JAK inhibitors as detailed in the DHPC letter (Q26-Q27).

In addition, information on the following was collected:

- Specialty (rheumatologist/dermatologist)
- Baricitinib prescriber status (yes, have previously prescribed/have not yet prescribed)
- Demographic information: geographic location (country)
- Clinical experience: duration of experience treating patients with relevant indication (years), number of patients for whom they have prescribed baricitinib (count).

9.5. Data Sources

In order to target the desired population, the data source selected, sourced from IQVIA (a subcontractor of UBC), consisted of dermatologists and rheumatologists in each of the selected countries who had previously agreed to be contacted for this type of research. Based on feasibility assessments of the list of dermatologists and rheumatologists from each of the participating countries, invitations were sent to all rheumatologists in each country's list. There were larger numbers of dermatologists listed in Germany and France, therefore, it was intended to conduct a 50% simple random sample in those 2 countries while all dermatologists in Sweden and Spain were to be invited. Section 9.9.5 describes how this sampling was not conducted and instead all dermatologists were invited from these countries.

Dermatologists and rheumatologists received an invitation letter via email and/or postal mail to participate in the survey. The invitation letter (Protocol, Appendix 1.1) included: an overview of the rationale for the survey, information on how to access the survey online and a unique invitation code to ensure that the invitation was used only once. Based on survey uptake within each respective country, reminder notices were sent via email and/or postal mail to those who were invited but had not yet participated. The database of invitees was regularly updated with responders and after each invitation mailing, the database was cross-checked with any correspondence that had an invalid address, was undeliverable or had incorrect contact details. Those who were sent an invitation, and there was no evidence that it had not been received (e.g., an invalid address), and who did not respond within 2 weeks from the initial mailing, received at least 1 reminder invitation.

A structured questionnaire was used to collect survey data (Protocol, Appendix 1.1). It comprised closed-ended questions or statements with multiple response choices.

The survey was voluntary. The collection of any personal, identifying information (e.g., first name, last name, address) from respondents was only used for processing of participants' financial compensation, as allowed by local laws and country regulations, and was stored in a separate database.

Each individual HCP was randomly assigned a unique code to access the survey. Each unique code was deactivated upon first use to prevent the code from being used to complete the survey

multiple times. Individuals did not have to actively "decline to complete the survey." Therefore, there was no ability to track those who decline to participate. Individuals who log into the survey and decline to complete the full survey were presented with two questions relating to whether non-respondents have prescribed baricitinib and whether they were aware of the important safety information communicated in the HCP Educational Materials and in the DHPC communication. Participants who agree to respond to the survey began with a screening module with questions to confirm eligibility.

The internet survey was self-administered. If a survey was started by the HCP but could not be completed due to any technical issues, the HCP could contact the SCC for a paper survey to be posted to the HCP to complete. This process was outlined in the Data Management Plan and SCC Plan. For both the internet and paper modalities, the surveys were available in the applicable local language.

The survey included questions in the following categories:

Screening questions:

- Agreement to participate
- Dermatologists or rheumatologists
- Current or past employment by Lilly, or any of its affiliates, UBC, IQVIA, the EMA, or any NCA

Data on demographic characteristics:

- Geographical location
- Years of experience in speciality
- Proportion of patients seen with relevant indication for the speciality (i.e., proportion of patients seen with either AD or AA for the dermatologists or proportion of patients seen with RA for the rheumatologists)
- Prescriber of baricitinib (yes/no)
- Number of patients prescribed baricitinib

Data pertaining to evaluation of the dermatologists and rheumatologists' understanding of the important safety information in the HCP Educational Materials, communication of the important safety information and mitigating actions to patients prescribed baricitinib for the first time, and distribution of the PAC to patients prescribed baricitinib for the first time.

Data pertaining to evaluation of dermatologists' and rheumatologists' understanding of the content of the DHPC.

9.6. Bias

A number of controls were in place to ensure that the survey was conducted to minimise bias, including the following:

- Lists of response options were randomised to minimise the potential for positional bias.

- The survey was programmed to ensure that questions were asked in the appropriate sequence, and all questions were presented in a standard order to reduce exposure bias. Respondents could not skip ahead or go back to a question once the question had been answered. All questions presented had to be answered in order to complete a survey.
- While it was not the preferred modality for completing the survey, if an HCP had technical difficulties with the internet survey, they could request a paper survey from the SCC. This introduced the inability to prevent respondents from going back to a previous question or skipping questions. As only a small number of paper survey requests was anticipated, this was not expected to be a major factor in the overall bias for the study.
- Respondents were provided with a unique code during the recruitment process in order to gain access to the internet-based systems. The code was inactivated after use to minimise exposure bias and fraud.

9.7. Study Size

The study targeted completion of approximately 400 surveys (approximately 200 dermatologists and approximately 200 rheumatologists), with at least 50% of those from dermatologists who had prescribed baricitinib and 50% from rheumatologists who had prescribed baricitinib. This provided an estimated precision of ±7% around the observed proportion of correct responses (for each specialty) who answer correctly, assuming the true proportion was 50%. If the true proportion was greater or lesser than 50%, the estimated proportion was more precise. The maximum number of completed surveys from any individual country was set to 80 dermatologists and 80 rheumatologists. A detailed justification of the sample size is in the Protocol in Section 9.5.

9.8. Data Transformation

The categorisation of variables by subgroup (speciality, country of practice, prescribing status, prescribing number of patients treated, prescriber experience, and survey reset status) are further described in Section 9.9.4.

9.9. Statistical Methods

Descriptions of the statistical methods herein are based on the Survey Analysis Plan (SAP), version 1.0, dated 28 August 2024.

9.9.1. Main Summary Measures

Statistical analyses were descriptive, i.e., no formal hypothesis was tested. Counts and percentages were calculated for each question/item in the questionnaire. All confidence intervals (CIs) around the percentages were exact two-sided 95% CIs calculated according to the method of Clopper-Pearson (Clopper and Pearson, 1934). The survey contains skip patterns, i.e., some questions were skipped depending on the answer to a previous question.

The analysis populations included:

All Respondents – The All Respondents Population consists of respondents that accessed the survey using a unique code. These respondents were used as the denominator for percentages in

survey administration statistics, unless otherwise specified, and in the survey eligibility results analysis.

Completed Surveys (Primary Population) – The population for all remaining analyses includes only those with completed surveys. "Completed" was defined as an eligible respondent who completed all questions/items. An eligible respondent was defined as one who completed all eligibility questions, has met all inclusion criteria and none of the exclusion criteria.

Of note: as outlined in the protocol and Section 9.2, no more than 80 respondents were to be included from a specialty within any 1 country. By error, more than the planned 80 dermatologists completed the survey in Germany. A total of 131 dermatologists completed the survey from Germany, 51 more than the protocol allowed. The primary analysis maintained the protocol-defined strategy and restricted to only the first 80 completers from Germany. However, a post-hoc sensitivity analysis was performed where all respondents completing the survey were included to determine if the results from the additional respondents had any effect on the results of this survey. This is referred to as the "Completed Surveys including all Respondents from Germany."

9.9.2. Main Statistical Methods

Analysis of the Primary Objectives

All responses to questions around the objectives were summarised using counts and percentages in the completed survey population (primary population) stratified by country and overall. Exact binomial two-sided 95% CI were calculated for the proportion of respondents who gave the correct or desired responses.

Survey data were analysed overall, and then by subgroups further described in Section 9.9.4. For Objective 1, Table 9.1. Key Risk Messages and Criteria for Success for Objective 1 (Healthcare Professional Educational Materials) outlines the 7 KRM within the HCP Educational Materials, the individual questions within each message, and the criteria for success of each message. In short, the 7 KRMs were the following:

- KRM#1: Pregnancy (Q8)
- KRM#2: Lipid parameters (Q9)
- KRM#3: Infections (Q10, Q11, Q12)
- KRM#4: Venous thromboembolism (VTE) (Q13a, Q13b, and Q13c).
- KRM#5: MACE (Q14a, Q14b, and Q14c)
- KRM#6: Lymphoma and other Malignancies (Q15a, Q15b).
- KRM#7: Dosing (Q16a, Q16b, and Q16c).

To be counted as demonstrating of understanding of a specific KRM, all questions/items of the KRM must be answered correctly. The number and percentages, including exact binomial

two-sided 95% CIs, of respondents demonstrating understanding was calculated for each individual KRM and for all KRMs.

Table 9.1. Key Risk Messages and Criteria for Success for Objective 1 (Healthcare Professional Educational Materials)

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
KRM 1: Pregnancy	8a	Correctly responding to the single element of Question 8 for KRM 1.
Question 8: Which of the following statements is correct? *Select one only.*		
8a Olumiant (baricitinib) is contraindicated in pregnancy.		
8b Olumiant (baricitinib) is safe to use in pregnancy.		
8c Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment.		
8d I do not know.		
KRM 2: Lipid parameters	9a	Correctly responding to the single element of Question 9 for KRM 2.
Question 9: Which of the following statements is correct? *Please select one option.*		
9a In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected.		
9b There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing.		
9c I do not know.		
KRM 3: Infections	10a	Correctly responding to the three elements for Questions 10, 11, and 12 for KRM 3.
Question 10: Which of the following statements is true? *Please select one option.*		
10a Olumiant (baricitinib) increases the potential risk of infection.		
10b Patients can wait to mention any symptoms of infection at their next scheduled clinic visit.		
10c All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics.		
10d I do not know.		
Question 11: Which of the following statements is correct? *Select one only.*	11c	

Table 9.1. Key Risk Messages and Criteria for Success for Objective 1 (Healthcare Professional Educational Materials)

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
11a If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued.		
11b Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib).		
11c Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy.		
11d I do not know.		
Question 12: Which of the following statements is correct? *Select one only.*	12a	
12a Caution should be used when treating patients with diabetes with Olumiant (baricitinib).		
12b Olumiant (baricitinib) should never be used in patients over 65 years of age.		
12c I do not know.		
KRM 4: Venous thromboembolism		Correctly responding to the three elements of Question 13 for KRM 4.
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		
13a There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib).	False	
13b Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors.	True	
13c Patients should be advised to seek immediately medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism.	True	
KRM 5: Major Adverse Cardiovascular Events		Correctly responding to the three elements of Question 14 for KRM 5.
Question 14: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		

Table 9.1. Key Risk Messages and Criteria for Success for Objective 1 (Healthcare Professional Educational Materials)

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
14a There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib).	True	
14b Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors.	False	
14c In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available.	True	
KRM 6: Lymphoma and other Malignancies		Correctly responding to the two elements of Question 15 for KRM 6.
Question 15: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		
15a Lymphoma or other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib).	True	
15b In patients with a past history of malignancy or with other malignancy risk factors, Olumiant (baricitinib) should only be used if no suitable alternative treatments are available.	True	
KRM 7: Dosing		Correctly responding to the three elements of Question 16 for KRM 7
Question 16: For which patients is a 2 mg once daily dose recommended? *Please answer True, False, or I do not know for each of the following statements.*		
16a Patients aged 65 years or over.	True	
16b Patients with depression.	False	
16c Patients at a higher risk of malignancy, venous thromboembolism, and major adverse cardiovascular events or with a history of chronic or recurrent infections.	True	

The relevant questions to define success for Objective 2 were based on 1 KRM regarding the JAK inhibitor class effects (Q17, Q18, Q19). To be counted as demonstrating understanding of KRM #8 regarding class effects, all questions/items in this KRM must be answered correctly as shown in Table 9.2. Key Risk Messages and Criteria for Success for Objective 2 (Direct Healthcare Professional Communication).

Table 9.2. Key Risk Messages and Criteria for Success for Objective 2 (Direct Healthcare Professional Communication)

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
KRM 8: JAK inhibitor class effect		Correctly responding to the 6 elements of Questions 17, 18 and 19 for KRM 8
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? *Please answer True, False, or I don't know for each of the following statements.*		
17a Major adverse cardiovascular events.	True	
17b Venous thromboembolism.	True	
17c Serious infections.	True	
17d Mortality.	True	
Question 18. Which of the following statements is correct? *Select one only.*	18b	
18a Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression.		
18b Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy.		
18c Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes.		
18d I do not know.		
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*	19a	
19a Periodic skin examination.		
19b Periodic liver ultrasound.		
19c I do not know.		

Analysis of Additional Survey Questions

All other questions including demographics, inclusion/exclusion questions to confirm respondent eligibility, prescribing status, clinical experience, and questions of safe use (such as communication of information to patients) were also analysed. The number and percentage of respondents were summarised by their responses to each question.

9.9.3. Missing Values

In order to minimise bias, the online survey was programmed to ensure respondents could not skip ahead and only allowed for missing data when caused by skip patterns. To be considered in the Primary Population for analysis, the online survey had to be completed entirely, thus no missing data.

However, on paper surveys, there was a possibility of missing data not associated with skip patterns and the SCC could skip any question not completed by the respondent for the entry of paper surveys in the electronic data capture (EDC). The response to questions where the respondent checked multiple response options instead of one, was entered in the EDC as missing and not included in the analysis.

9.9.4. Subgroup and Sensitivity Analyses

In addition to the overall analysis, survey data of the objectives on all completed surveys were analysed stratified by the following sub-groups, as applicable.

Subgroup analysis: Specialty

- Rheumatologist
- Dermatologist

Subgroup analysis: Country of practice:

- Sweden
- France
- Germany
- Spain

Subgroup analysis: Prescribing status

- Active prescriber (has previously prescribed)
- Potential prescriber (has not previously prescribed baricitinib)

Subgroup analysis: Prescribing number of patients treated

- High prescribers
- Low prescribers

The cut-off between low and high prescribers was based on the distribution of the number of patients treated in the completed surveys. The goal was to have similar sample sizes in both sub-groups. The definition of both prescribers categories was as follows: Low prescribers: ≤ 5 patients in the last 6 months; High prescribers: ≥ 6 patients in the last 6 months.

Subgroup analysis: Prescriber experience

- High experience
- Medium experience
- Low experience

Prescriber experience was based on the responses to survey Question 4 (number of years treating patients with AD: <5, 5-10, 11-15, >15 years) and Question 5 (proportion of patients who have AD/AA or RA: 0-25%, 26-50%, 51-75%, 76-100%). Low, medium, and high experience was defined post-hoc based on the actual distribution of Question 4 and Question 5. The target was to construct 3 categories of similar sample size. The following approach served as a starting point for the definition of the 3 experience categories:

- High experience: prescriber with >15 years experience and 51-75% or 76-100% AD/AA or RA patients.
- Low experience: prescribers with <5 years experience and 0-25% or 26 to 50% AD/AA or RA patients, and
- Medium experience: all remaining prescribers.

Subgroup analysis: Survey reset status

- No Survey Reset
- Survey Reset

If a survey has been started by the HCP but could not be completed due to any technical issues, the HCP could contact the SCC for a paper survey to complete. This process was outlined in the Data Management Plan and SCC Plan. This subgroup analysis was only performed if 5% or more of the completed surveys had been completed by paper if only partially completed online.

9.9.5. Amendments to the Protocol or Statistical Analysis Plan

Differences in study execution from what was detailed in the protocol are described below.

- The protocol planned that a 50% random sample of dermatologists would be selected and invited from Germany and France while all dermatologists in Sweden and Spain were to be invited because there were larger numbers of dermatologists than rheumatologists listed in Germany and France. However, this random sampling was erroneously not conducted and all available dermatologists and rheumatologists on the list were invited from all countries.
- The protocol had specified that the maximum responding HCPs for a speciality within a country was 80. An error in the survey programming did not turn off responses once 80 respondents were achieved in a given specialty for a country. Hence the error described in Section 9.9.1 where more than 80 dermatologists in Germany responded. Corrections into survey administration were put in place to avoid this occurring in an additional specialty. The primary analysis maintained the sample size limits described in the protocol with a post-hoc sensitivity analysis that included the oversampled German dermatologists. This sensitivity analysis was not described in the protocol but was planned prior to finalisation of the SAP. The sensitivity analysis thus describes the results of the KRMs when including all respondents, not limiting to the protocol defined 80 maximum for a specialty within a country.
- In addition, during analysis of data, it was discovered that 3 dermatologists (2 from France and 1 from Spain) were misclassified under the wrong specialty based on

Question 3 of the survey. Given the inability to reconcile the correct specialty, the surveys from these 3 HCPs were excluded from the analysis.

- The protocol version b had described offering a call centre for completing the survey on the telephone. Due to unforeseen issues in establishing this modality for survey completion, protocol amendment (version c) instead described that HCPs encountering issues with electronic survey completion could call the UBC help number and request a paper survey to be mailed to them for completion.

9.10. Quality Control

Data were collected using a secure and validated online EDC system designed and built by UBC. A System Development Life Cycle (SDLC) was used for validation that complies with UBC internal Information Technology (IT) Standard Operating Procedures (SOPs). The SDLC was fortified with SOPs addressing validation for all clinical and risk minimisation-related applications. The internet-based repository was used to store survey data and other relevant programme information. UBC's IT applications are governed by a development approach to ensure compliance with the Food and Drug Administration 21 CFR Part 11, international regulations and standards (e.g., EU Good Pharmacovigilance Practice, International Council for Harmonisation) and relevant EMA guidelines. The system was compliant for the entry, storage, handling, analysis and transmission of electronic information. Respondent-identifying information was stored separately from the survey responses. At the end of each survey cycle, data were extracted from the EDC.

Programming was reviewed by UBC Quality Control and simulated users (User Acceptance Testing) prior to implementation.

At the completion of data collection, data were extracted from the EDC and mapped to Statistical Analysis Software (SAS) datasets (SAS V9.1.3 or higher). The extracted EDC data was mapped to SAS datasets ("original" production datasets) as defined in the annotated Data Collection Tools (aDCTs) by a SAS programmer/designee. The mapping of raw data was validated, as was the programming of the analysis tables created from the raw EDC data. Additionally, the EDC data was also mapped to SAS datasets by a Server Reporting Services programmer as defined in the aDCTs and validated by the UBC Quality Control Team. These original SAS datasets were validated by double programming and Quality Control. The validated original SAS datasets were then used by a SAS programmer to create a set of summary tables and listings according to the SAP text and mock-up tables. If derived analysis datasets were required to produce these summary tables, these were created and independently validated. All tables, listings, and figures output were independently validated and documented. Summary tables were reviewed by the appropriate team members and included in the final report sent to Lilly to be submitted to the PRAC.

UBC has an IT Quality Assurance Group that was responsible for managing and overseeing system/application development and validation, as well as related compliance functions.

10. Results

10.1. Participants

Survey administration statistics for rheumatologists and dermatologists invited to participate in the survey are presented by country and overall in Table 10.1. Survey Administration Statistics. All supporting tables are provided in Appendix 1.2.

Rheumatologists

A total of 11,858 survey invitations and reminder letters were sent to rheumatologists involved in the treatment and management of patients with RA.

Of those invited, 290 (2.4%) responded to the invitation using their unique identification. Of the 290 respondents, 268 (92.4%) were eligible for participation and of those, 248 (85.5%) respondents completed the survey (28 from Sweden, 81 from France, 80 from Germany, and 59 from Spain).

Dermatologists

A total of 23,591 survey invitations and reminder letters were sent to dermatologists involved in the treatment and management of patients with AD.

Of those invited, 388 (1.6%) responded to the invitation using their unique identification. Of the 388 respondents, 350 (90.2%) were eligible for participation and of those, 333 (85.8%) respondents completed the survey (46 from Sweden, 72 from France, 131 from Germany, and 84 from Spain).

A total of 438 survey invitations were returned by respondents and the majority were from France (n=384).

As outlined in the protocol and Section 9.2, no more than 80 respondents were to be included from any 1 country. Of the 333 dermatologists who completed the survey, 131 were from Germany. Because this was 51 more respondents for a country than the protocol allowed, a post-hoc sensitivity analysis was conducted including all German respondents to determine if the results from the additional respondents had any effect on the results of this survey. Only the first 80 were included in the primary analysis to match protocol specifications. In addition, there were 84 dermatologists from Spain who completed the survey which exceeded the 80 dermatologists allowed per protocol. The 84 respondents from Spain were included in the primary analysis as the extra 4 surveys were considered too few respondents to appreciably change the study results.

Per protocol, if the respondents had difficulty completing the online survey, they could request a paper survey. Of the completed surveys, 5 paper surveys were received and entered into the electronic data system by a clinical research associate: 1 from France (Rheumatologist), 2 from Sweden (Dermatologists), 1 from Sweden (Rheumatologist), and 1 from Spain (Dermatologist).

Table 10.1. Survey Administration Statistics

Parameter, n (%)	Sweden	France	Germany	Spain	Overall
Rheumatologists					
Number of Survey invitations[a]	1,100	4,811	4,242	1,705	11,858
All Respondents[b]	35 (3.2)	88 (1.8)	95 (2.2)	72 (4.2)	290 (2.4)
Eligible Respondents[d]	31 (88.6)	83 (94.3)	88 (92.6)	66 (91.7)	268 (92.4)
Completed the survey[d]	28 (80.0)	81 (92.0)	80 (84.2)	59 (81.9)	248 (85.5)
Did not complete the survey[d]	3 (8.6)	2 (2.3)	8 (8.4)	7 (9.7)	20 (6.9)
Respondents not eligible[c, d]	4 (11.4)	5 (5.7)	7 (7.4)	6 (8.3)	22 (7.6)
Dermatologists					
Number of Survey invitations[a]	1,700	10,296	8,386	3,209	23,591
All Respondents[b]	52 (3.1)	83 (0.8)	151 (1.8)	102 (3.2)	388 (1.6)
Eligible Respondents[d]	49 (94.2)	72 (86.7)	140 (92.7)	89 (87.3)	350 (90.2)
Completed the survey[d]	46 (88.5)	72 (86.7)	131[e] (86.8)	84 (82.4)	333 (85.8)
Did not complete the survey[d]	3 (5.8)	0	9 (6.0)	5 (4.9)	17 (4.4)
Respondents not eligible[c, d]	3 (5.8)	11 (13.3)	11 (7.3)	13 (12.7)	38 (9.8)
Number of survey invitations returned (includes both rheumatologists and dermatologists)	11	384	43	0	438

Source: Appendix 1.2, Table 1.1

[a] Number of total survey invitations sent, including reminder invitations sent when an HCP had not yet responded.

[b] Number of respondents who accessed the survey. Percentage is based on the number of invitations provided to HCPs.

[c] Number of respondents who did not meet eligibility criteria or did not complete eligibility questions. The responses to the eligibility criteria with the reason for ineligibility are presented in Table 10.2. Survey Participant Eligibility Results - All Respondents.

[d] Percentages are based on the number of all respondents.

[e] While 131 dermatologists from Germany completed the survey, only the first 80 were included in the primary analysis to match protocol specifications. A sensitivity analysis of the KRM understanding by country includes all 131 respondents.

Survey participant eligibility results for rheumatologists and dermatologists who responded to the survey are presented by country and overall in Table 10.2. Survey Participant Eligibility Results - All Respondents.

Of the 678 respondents who responded to the survey, 37 did not agree to take the survey. Of the 641 who did agree to participate, 41 were not eligible because they did not complete all of the questions, 15 indicated that they or an immediate family member had worked directly for Lilly or its affiliates, UBC, the EMA, or any NCA; and 4 respondents were not rheumatologists or

dermatologists. Of the remaining 581 respondents, the last 51 respondents who completed the survey from Germany were not included in the primary analysis (N=530; Section 10.3).

Table 10.2. Survey Participant Eligibility Results - All Respondents

Question	Sweden (N=87) n (%)	France (N=171) n (%)	Germany (N=246) n (%)	Spain (N=174) n (%)	Overall (N=678) n (%)
Question 1: Do you agree to take part in this survey about Olumiant® (baricitinib)?					
Yes	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
No	0	0	0	0	0
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 1a: Have you ever prescribed Olumiant?					
Yes	0	0	0	0	0
No	0	0	0	0	0
Prefer not to answer	0	0	0	0	0
N/A (answered 'Yes' to Question 1)	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 1b: Are you familiar with the important safety information included in the Olumiant Healthcare Professional Educational Materials?					
Yes	0	0	0	0	0
No	0	0	0	0	0
Prefer not to answer	0	0	0	0	0
N/A (answered 'Yes' to Question 1)	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 1c: Are you familiar with the important safety information included in the recent letter to communicate safety regarding all Janus kinase (JAK) inhibitors of [16 March 2023 France; 17 March 2023 Germany; 21 March 2023 Sweden]					
Yes	0	0	0	0	0
No	0	0	0	0	0
Prefer not to answer	0	0	0	0	0
N/A (answered 'Yes' to Question 1)	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 2: Have you or any of your immediate family members ever worked directly for Eli Lilly and Company (Lilly) or its affiliates, United BioSource, LLC (UBC), IQVIA, the European Medicines Agency (EMA), or any National Competent Authority (NCA)?					
Yes[a]	2 (2.3)	3 (1.8)	2 (0.8)	8 (4.6)	15 (2.2)
No	81 (93.1)	157 (91.8)	230 (93.5)	156 (89.7)	624 (92.0)
Discontinued	4 (4.6)	11 (6.4)	14 (5.7)	10 (5.7)	39 (5.8)

Table 10.2. Survey Participant Eligibility Results - All Respondents

Question	Sweden (N=87) n (%)	France (N=171) n (%)	Germany (N=246) n (%)	Spain (N=174) n (%)	Overall (N=678) n (%)
Question 3: What is your practising speciality?					
Dermatologist	49 (56.3)	74 (43.3)	140 (56.9)	89 (51.1)	352 (51.9)
Rheumatologist	31 (35.6)	83 (48.5)	88 (35.8)	66 (37.9)	268 (39.5)
Other[a]	1 (1.1)	0	2 (0.8)	1 (0.6)	4 (0.6)
Question not asked[b]	2 (2.3)	3 (1.8)	2 (0.8)	8 (4.6)	15 (2.2)
Discontinued	4 (4.6)	11 (6.4)	14 (5.7)	10 (5.7)	39 (5.8)
Question 6: Have you prescribed Olumiant (baricitinib)?					
Yes	55 (63.2)	127 (74.3)	197 (80.1)	139 (79.9)	518 (76.4)
No	25 (28.7)	28 (16.4)	31 (12.6)	16 (9.2)	100 (14.7)
Question not asked[b]	3 (3.4)	3 (1.8)	4 (1.6)	9 (5.2)	19 (2.8)
Discontinued	4 (4.6)	13 (7.6)	14 (5.7)	10 (5.7)	41 (6.0)

Source: Appendix 1.2, Table 1.2

Note: This table includes all dermatologists from Germany who completed the survey.

Note: Respondents are designated "discontinued" if they did not answer all eligibility questions and were not identified as ineligible based on responses to previous questions. Once respondents were designated as "discontinued," they were counted as such in all subsequent eligibility questions.

Note: Question 1a, 1b and 1c have been answered by only those not agreeing to participate in survey.

[a] These responses were not consistent with survey eligibility and thus indicated the HCP was ineligible to participate in the survey.

[b] Question not asked due to the skip pattern in the survey or previous question termination.

10.2. Descriptive Data

Description of eligible respondents who completed the survey by country and overall is presented in Table 10.3. Description of Eligible Respondents - Completed Surveys. This cohort of 530 respondents includes only the first 80 of 131 dermatologists completing the survey from Germany as the primary analysis per protocol.

Of the 530 respondents who completed the survey, a similar proportion indicated they were practising for less than 5 years (25.7%), 5 to 10 years (29.4%), or more than 15 years (27.0%); the smallest proportion were practising for 11 to 15 years (17.9%) (Q4). Most dermatologists treated either 5 to 25 patients per month (51.8%) or more than 25 patients per month (44.3%) (Q5a). Most rheumatologists treated more than 25 patients per month (71.0%) followed by 5 to 25 patients per month (26.2%) (Q5b). Most respondents (83.4%) indicated they had prescribed baricitinib (Q6). Of those who had prescribed baricitinib, 50.5% had treated 1 to 5 patients, 24.4% more than 10 patients, and 21.9% between 6 to 10 patients with baricitinib within the last 6 months (Q7).

Table 10.3. Description of Eligible Respondents - Completed Surveys

Question	Sweden (N=74) n (%)	France (N=153) n (%)	Germany (N=160) n (%)	Spain (N=143) n (%)	Overall (N=530) n (%)
Question 4: In total, how many years have you been practicing in your specialty?					
Less than 5 years	18 (24.3)	38 (24.8)	40 (25.0)	40 (28.0)	136 (25.7)
5 – 10 years	26 (35.1)	45 (29.4)	43 (26.9)	42 (29.4)	156 (29.4)
11 – 15 years	11 (14.9)	24 (15.7)	31 (19.4)	29 (20.3)	95 (17.9)
More than 15 years	19 (25.7)	46 (30.1)	46 (28.8)	32 (22.4)	143 (27.0)
Question 5a: Approximately, how many patients per month do you see who have either atopic dermatitis or alopecia areata?[a]					
Less than 5	1 (2.2)	5 (6.9)	3 (3.8)	2 (2.4)	11 (3.9)
5-25	34 (73.9)	46 (63.9)	34 (42.5)	32 (38.1)	146 (51.8)
>25	11 (23.9)	21 (29.2)	43 (53.8)	50 (59.5)	125 (44.3)
N/A (answered 'Rheumatologist' to Question 3)	28	81	80	59	248
Question 5b: Approximately, how many patients per month do you see who have rheumatoid arthritis?[a]					
0-5	0	6 (7.4)	0	1 (1.7)	7 (2.8)
5-25	5 (17.9)	41 (50.6)	4 (5.0)	15 (25.4)	65 (26.2)
>25	23 (82.1)	34 (42.0)	76 (95.0)	43 (72.9)	176 (71.0)
N/A (answered 'Dermatologist' to Question 3)	46	72	80	84	282
Question 6: Have you prescribed Olumiant (baricitinib)?					
Yes	51 (68.9)	125 (81.7)	138 (86.3)	128 (89.5)	442 (83.4)
No	23 (31.1)	28 (18.3)	22 (13.8)	15 (10.5)	88 (16.6)
Question 7: Approximately, how many patients have you treated in the last six months with Olumiant (baricitinib)?[a]					
None	1 (2.0)	10 (8.0)	1 (0.7)	2 (1.6)	14 (3.2)
1-5	38 (74.5)	75 (60.0)	57 (41.3)	53 (41.4)	223 (50.5)
6-10	8 (15.7)	24 (19.2)	29 (21.0)	36 (28.1)	97 (21.9)
More than 10	4 (7.8)	16 (12.8)	51 (37.0)	37 (28.9)	108 (24.4)
N/A (answered 'No' to Question 6)	23	28	22	15	88

Source: Appendix 1.2, Table 2

Note: This table includes only the first 80 dermatologists completing the survey from Germany.

[a] Question was not asked to select respondents due to skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Responses to questions about the HCP Educational Material for baricitinib by eligible respondents who completed the survey are presented in Table 10.4. Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) - Completed Surveys.

Of the 530 respondents who completed the survey, 52.1% indicated that they were previously aware of the Health Professional Educational Material for baricitinib (Q20). Among those respondents indicating awareness, 60.9% indicated that they received a copy of the Health Professional Educational Material for baricitinib (Q21) and of those who received a copy, 75.6% indicated reading it (Q22).

Of 530 respondents, 69.1% indicated they received a copy of the DHPC to communication safety regarding all JAK inhibitors (Q26), and 88.8% of those respondents indicated reading it (Q27).

Table 10.4. Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) - Completed Surveys

Question	Respondents (N=530) n (%)
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?	
Yes	276 (52.1)
No	254 (47.9)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)? [a]	
Yes	168 (60.9)
No	44 (15.9)
I don't remember	64 (23.2)
N/A (Answered "No" to Question 20)	254
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)? [a]	
Yes	127 (75.6)
No	23 (13.7)
I don't remember	18 (10.7)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	362
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?	
Yes	366 (69.1)
No	81 (15.3)
I don't know	83 (15.7)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]	
Yes	325 (88.8)
No	29 (7.9)
I don't know	12 (3.3)
N/A (Answered "No" or "I don't know" to Question 26)	164

Source: Appendix 1.2, Table 6

Note: This table includes only the first 80 dermatologists completing the survey from Germany.

[a] Question was not asked to select respondents due to skip patterns based on response to previous question. Therefore, counts and percentages shown are of respondents who were administered this question.

10.3. Main Results

10.3.1. Individual Questions about Important Safety Information

Responses to the individual questions related to the understanding of the important safety information by eligible respondents who completed the survey are presented in Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys.

Of the 530 eligible respondents who completed the survey, many correctly indicated that baricitinib is contraindicated in pregnancy (73.0%) (Q8).

A high percentage of respondents correctly indicated that lipid parameters should be monitored and hyperlipidaemia managed, if detected, (90.4%) (Q9), that baricitinib increases the potential risk of infection (95.7%) (Q10), that patients should be screened for viral hepatitis and active tuberculosis should be ruled out before baricitinib therapy (94.7%) (Q11). The majority correctly indicated that caution should be used when treating diabetic patients with baricitinib (78.3%) (Q12).

A high percentage of respondents correctly responded “False” to the statement: “There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving baricitinib” (83.8%) (Q13a); “True” to the statement: “Baricitinib should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors” (97.2%) (Q13b); and “True” to the statement: “Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism (99.6%) (Q13c). Most respondents also correctly answered “True” when prompted with the following statement: “There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including baricitinib” (91.5%) (Q14a). A slightly lower percentage of respondents correctly indicated “False” when prompted with the statement: “Baricitinib is contraindicated in patients with cardiovascular risk factors” (66.8%) (Q14b) and correctly responded “True” to the statement: “In patients who are past or current smokers, baricitinib should only be used if no suitable treatment alternatives are available” (77.2%) (Q14c).

Many respondents correctly responded “True” to the statements “Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including baricitinib” (71.7%) (Q15a) and “In patients with a past history of malignancy or with other malignancy risk factors baricitinib should only be used if no suitable alternative treatments are available” (88.3%) (Q15b).

When asked for which patients is a 2 mg once daily dose recommended, many respondents correctly responded “True” to the prompts indicating “Patients aged 65 years or older” (79.4%) (Q16a) and “Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections” (73.4%) (Q16c), and many correctly responded “False” to the prompt indicating “Patients with depression” (74.0%) (Q16b).

When asked to identify events with an increased incidence observed with JAK inhibitor treatment compared to tumour necrosis factor alpha (TNFα) inhibitors, most respondents correctly responded "True" to the prompt indicating "Major adverse cardiovascular events" (80.6%) (Q17a) and "Venous thromboembolism" (92.1%) (Q17b), while a lower proportion correctly responded "True" to the prompts indicating "Serious infections" (29.2%) (Q17c) and "Mortality" (18.5%) (Q17d).

Many respondents identified the correct statements that "Compared to TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy" (60.6%) (Q18) and that for patients treated with baricitinib, "Periodic skin examination" is recommended (78.3%) (Q19).

Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
Question 8: Which of the following statements is correct? *Select one only.*	
Olumiant (baricitinib) is contraindicated in pregnancy[a]	387 (73.0) [69.0-76.8]
Olumiant (baricitinib) is safe to use in pregnancy	7 (1.3)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	105 (19.8)
I do not know.	31 (5.8)
Question 9: Which of the following statements is correct? *Please select one option.*	
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	479 (90.4) [87.5-92.8]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	31 (5.8)
I do not know	20 (3.8)
Question 10: Which of the following statements is true? *Please select one option.*	
Olumiant (baricitinib) increases the potential risk of infection[a]	507 (95.7) [93.6-97.2]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	11 (2.1)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0
I do not know	12 (2.3)
Question 11: Which of the following statements is correct? *Select one only.*	
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	2 (0.4)
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	16 (3.0)

Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	502 (94.7) [92.5-96.5]
I do not know	10 (1.9)
Question 12: Which of the following statements is correct? *Select one only.*	
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	415 (78.3) [74.5-81.7]
Olumiant (baricitinib) should never be used in patients over 65 of age	65 (12.3)
I do not know	50 (9.4)
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*	
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)	
True	59 (11.1)
False[a]	444 (83.8) [80.4-86.8]
I don't know	27 (5.1)
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors	
True[a]	515 (97.2) [95.4-98.4]
False	10 (1.9)
I don't know	5 (0.9)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism	
True[a]	528 (99.6) [98.6-100.0]
False	0
I don't know	2 (0.4)
Question 14: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*	
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)	
True[a]	485 (91.5) [88.8-93.7]
False	31 (5.8)
I don't know	14 (2.6)
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors	
True	154 (29.1)

Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
False[a]	354 (66.8) [62.6-70.8]
I don't know	22 (4.2)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available	
True[a]	409 (77.2) [73.4-80.7]
False	89 (16.8)
I don't know	32 (6.0)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***	
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)	
True[a]	380 (71.7) [67.7-75.5]
False	76 (14.3)
I don't know	74 (14.0)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available	
True[a]	468 (88.3) [85.3-90.9]
False	34 (6.4)
I don't know	28 (5.3)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***	
16a: Patients aged 65 years or over	
True[a]	421 (79.4) [75.7-82.8]
False	65 (12.3)
I don't know	44 (8.3)
16b: Patients with depression	
True	44 (8.3)
False[a]	392 (74.0) [70.0-77.7]
I don't know	94 (17.7)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections	
True[a]	389 (73.4) [69.4-77.1]
False	86 (16.2)

Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
I don't know	55 (10.4)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.	
17a: Major adverse cardiovascular events	
True[a]	427 (80.6) [76.9-83.9]
False	65 (12.3)
I don't know	38 (7.2)
17b: Venous thromboembolism	
True[a]	488 (92.1) [89.4-94.2]
False	25 (4.7)
I don't know	17 (3.2)
17c: Serious infections	
True[a]	155 (29.2) [25.4-33.3]
False	300 (56.6)
I don't know	75 (14.2)
17d: Mortality	
True[a]	98 (18.5) [15.3-22.1]
False	315 (59.4)
I don't know	117 (22.1)
Question 18: Which of the following statements is correct? *Select one only.*	
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	31 (5.8)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	321 (60.6) [56.3-64.8]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	38 (7.2)
I do not know	140 (26.4)
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*	
Periodic skin examination[a]	415 (78.3) [74.5-81.7]
Periodic liver ultrasound	44 (8.3)

Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
I do not know	71 (13.4)

Source: Appendix 1.2, Table 3

Note: 95% exact two-sided CIs are calculated using the Clopper-Pearson method.

Note: This table includes only the first 80 dermatologists completing the survey from Germany.

[a] Correct response.

10.3.2. Understanding of Key Risk Messages

Objective 1

The effectiveness of the important safety information from the HCP Educational Materials and PAC within Questions 8 through 16 were combined into 7 KRMs:

- KRM#1: Pregnancy (Q8)
- KRM#2: Lipid parameters (Q9)
- KRM#3: Infections (Q10, Q11, Q12)
- KRM#4: VTE (Q13a, Q13b, and Q13c).
- KRM#5: MACE (Q14a, Q14b, and Q14c)
- KRM#6: Lymphoma and other malignancies (Q15a, Q15b).
- KRM#7: Dosing (Q16a, Q16b, and Q16c).

As described in Section 9.9.2, to be counted as demonstrating understanding of a specific KRM, all questions/items of the KRM must have been answered correctly.

As shown in Table 10.6. Understanding the Key Risk Messages for Objective 1 - Completed Surveys,

- 387 respondents (73.0%) demonstrated understanding of KRM 1
- 479 (90.4%) demonstrated understanding of KRM #2
- 389 (73.4%) demonstrated understanding of KRM #3
- 434 (81.9%) demonstrated understanding of KRM #4
- 254 (47.9%) demonstrated understanding of KRM #5
- 350 (66.0%) demonstrated understanding of KRM #6
- 280 (52.8%) demonstrated understanding of KRM #7.

The proportion of responding HCPs that correctly answered all 16 items contributing to the 7 KRMs for Objective 1 was 14.3%. Demonstrating understanding of a single KRM required answering all questions/items of the respective key message correctly. Therefore, demonstrating understanding of all KRMs required the respondent to have answered all elements of all KRMs correctly. In other words, this reflects the proportion of that scored perfectly for all elements of Questions 8 through 16.

Table 10.6. Understanding the Key Risk Messages for Objective 1 - Completed Surveys

	Respondents (N=530) n (%) [95% CI]
KRM#1 Pregnancy (Q8)[a]	
Yes	387 (73.0) [69.0-76.8]
No	143 (27.0)
KRM#2 Lipid parameters (Q9)[b]	
Yes	479 (90.4) [87.5-92.8]
No	51 (9.6)
KRM#3 Infections (Q10, Q11, Q12)[c]	
Yes	389 (73.4) [69.4-77.1]
No	141 (26.6)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]	
Yes	434 (81.9) [78.3-85.1]
No	96 (18.1)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]	
Yes	254 (47.9) [43.6-52.3]
No	276 (52.1)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]	
Yes	350 (66.0) [61.8-70.1]
No	180 (34.0)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]	
Yes	280 (52.8) [48.5-57.1]
No	250 (47.2)
Understanding all KRMs for Objective 1	
Yes	**76 (14.3) [11.5-17.6]**
No	**454 (85.7)**

Source: Appendix 1.2, Table 4

Note: 95% exact two-sided CIs are calculated using the Clopper-Pearson method.

Note: This table includes only the first 80 dermatologists completing the survey from Germany.

[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.

[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.

[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.

[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.

[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.

[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.

[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Objective 2

The effectiveness of the DHPC distributed to dermatologists and rheumatologists within Questions 17 through 19 were combined into 1 KRM (KRM #8).

- The relevant questions to define success for Objective 2 were based on KRM #8 regarding the JAK inhibitor class effects (Q17, Q18, Q19).

For being counted as demonstrating understanding of KRM #8 regarding class effects, all questions/items in this KRM must be answered correctly (Table 10.7. Understanding the Key Risk Messages for Objective 2 - Completed Surveys).

The proportion of responding HCPs that responded correctly to all 6 items for KRM #8 for Objective 2 was 7.5%.

Table 10.7. Understanding the Key Risk Messages for Objective 2 - Completed Surveys

	Respondents (N=530) n (%) [95% CI]
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]	
Yes	40 (7.5) [5.4-10.1]
No	490 (92.5)

Source: Appendix 1.2, Table 5
Note: 95% exact two-sided CIs are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] To be counted as understanding of KRM #8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

10.3.3. Communication of Important Safety Information

Responses to the question about the communication of important safety information to patients prescribed baricitinib by eligible respondents who completed the survey are presented in Table 10.8. Communication of the Important Safety Information to Patients Prescribed Baricitinib for the First Time – Completed Surveys.

Of 530 total respondents, 190 indicated they had both prescribed baricitinib (Q6) and were previously unaware of the PAC for baricitinib (Q23). Among these 190 respondents, 92.6% indicated that someone in their practice/hospital communicates the important safety information to their patients when prescribing baricitinib for the first time (Q24).

Table 10.8. Communication of the Important Safety Information to Patients Prescribed Baricitinib for the First Time – Completed Surveys

Question	Respondents (N=530) n (%)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]	
Yes	176 (92.6)
No	12 (6.3)
I don't know	2 (1.1)
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	340

Source: Appendix 1.2, Table 6

Note: This table includes only the first 80 dermatologists completing the survey from Germany.

[a] Question was not asked to select respondents due to skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

10.3.4. Distribution of the Patient Alert Card

Responses to questions about the PAC for baricitinib by participants who completed the survey are presented in Table 10.9. Responses to Questions about the Patient Alert Card for Baricitinib for the First Time – Completed Surveys.

Of 530 respondents, 277 (52.3%) indicated that prior to the day of survey participation, they were aware of the PAC for baricitinib. Among 176 respondents indicating that they prescribe baricitinib (Q6) and that someone in their practice/hospital communicates important safety information to their patients when prescribing baricitinib for the first time (Q24), 15 (8.5%) indicated that when prescribing baricitinib for the first time, their patient would be provided with a PAC (Q25).

Table 10.9. Responses to Questions about the Patient Alert Card for Baricitinib for the First Time – Completed Surveys

Question	Respondents (N=530) n (%)
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?	
Yes	277 (52.3)
No	253 (47.7)
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]	
Yes	15 (8.5)
No	141 (80.1)
I don't know	20 (11.4)
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	354

Source: Appendix 1.2, Table 6

Note: This table includes only the first 80 dermatologists completing the survey from Germany.

[a] Question was not asked to select respondents due to skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

10.4. Subgroup Analyses

Subgroup analyses of responses to each individual question related to the understanding of the important safety information and of understanding of the KRMs were conducted by stratifying the results according to country of practice, prescribing status, prescriber specialty, prescribing frequency, and prescriber experience (as described in Section 9.9.4). The subgroup analyses were performed using the population that includes the 51 additional dermatologists from Germany. Both electronic and paper surveys were included in the subgroup analyses. The full set of subgroup tables are provided in Annex 1, Appendix 1.2.

Country of practice

When stratifying participants' responses by country of practice, differences (based on non-overlapping CIs) between responses of participants were noted for the following Questions by country (Source Table 3.1):

Question 12: *Please select one option. Which of the following statements is true? Response: Caution should be used when treating patients with diabetes with Olumiant (baricitinib).* Differences between Sweden and France versus Spain were noted favouring respondents from Spain (correct response rate 87.4% [80.8%-92.4%]) over respondents from Sweden (correct response rate 70.3% [58.5%-80.3%]) and France (correct response rate 73.9% [66.1%-80.6%]).

Question 14c: *Please select True [correct response] or False or I don't know. In patients who are past or current smokers, baricitinib should only be used if no suitable treatment alternatives are available.*

- Differences between Sweden versus France and Germany were noted favouring France (correct response rate 88.9% [82.8%-93.4%]) and Germany (correct response rate 82.5% [75.7%-88.0%]) over Sweden (correct response rate 63.5% [51.5%-74.4%]).
- Differences between France versus Spain and the Overall group were noted favouring France (correct response rate 88.9% [82.8%-93.4%]) over Spain (correct response rate 65.7% [57.3%-73.5%]) and the Overall group (correct response rate 77.2% [73.4%-80.7%]).
- Differences between Germany and Spain were noted favouring Germany (correct response rate 82.5% [75.7%-88.0%]) over Spain (correct response rate 65.7% [57.3%-73.5%]).

Question 16a: *Please select True [correct response] or False or I don't know. For patients aged 65 years or over a 2 mg once daily dose is recommended*. Differences between Germany and Spain were noted favouring Spain (correct response rate 87.4% [80.8%-92.4%]) over Germany (correct response rate 72.5% [64.9%-79.3%]).

Question 16c: *Please select True [correct response] or False or I don't know. For patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections a 2 mg once daily dose is recommended*.

- Differences between Sweden, Germany, and the Overall group versus Spain were noted favouring Spain (correct response rate 86.0% [79.2%-91.2%]) over Sweden (correct response rate 63.5% [51.5%-74.4%]) and Germany (correct response rate 65.0% [57.1%-72.4%]) and the Overall group (correct response rate 73.4% [69.4%-77.1%]).

By prescribing status

When stratifying participants' responses by prescribing status, differences (based on non-overlapping CIs) between responses of participants were noted for the following Questions, all favouring active prescribers over potential prescribers (Source Table 3.2):

Question 9: *Which of the following statements is correct? (Please select one option). Response: In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia manged, if detected*. A difference was noted by prescribing status favouring active prescribers (correct response rate 92.4% [89.7%-94.6%]) over potential prescribers (correct response rate 75.8% [65.9%-84.0%]).

Question 14c: *Please select True [correct response] or False or I don't know. In patients who are past or current smokers, baricitinib should only be used if no suitable treatment alternatives are available*. A difference was noted by prescribing status favouring active prescribers (correct response rate 79.0% [75.1%-82.5%]) over potential prescribers (correct response rate 64.2% [53.7%-73.8%]).

Question 16a: *Please select True [correct response] or False or I don't know. For patients aged 65 years or over a 2 mg once daily dose is recommended*. A difference was noted by prescribing status favouring active prescribers (correct response rate 82.1% [78.4%-85.4%]) over potential prescribers (correct response rate 64.2% [53.7%-73.8%]).

Question 16b: *Please answer True or False [correct response] or I don't know. For patients with depression a 2 mg once daily dose is recommended*. A difference was noted by prescribing status favouring active prescribers (correct response rate 76.1% [72.1%-79.9%]) over potential prescribers (correct response rate 68.2% [62.9%-73.1%]).

Question 16c: *Please select True [correct response] or False or I don't know. For patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections a 2 mg once daily dose is recommended*. A difference was noted by prescribing status favouring active prescribers (correct response rate 75.7% [71.7%-79.5%]) over potential prescribers (correct response rate 55.8% [45.2%-66.0%]).

By prescriber speciality

When stratifying participants' responses by prescriber specialty, differences (based on non-overlapping CIs) between responses of rheumatologists/dermatologists were noted for the following Questions (Source Table 3.3):

Question 9: *Which of the following statements is correct? (Please select one option). Response: In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia manged, if detected*. A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 94.0% [90.2%-96.6%]) over dermatologists (correct response rate 86.5% [82.3%-90.0%]).

Question 11: *Which of the following statements is correct? (Please select one option). Response: Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy*. A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 98.0% [95.4%-99.3%]) over dermatologists (correct response rate 92.5% [89.1%-95.1%]).

Question 14c: *Please answer True [correct response] or False or I don't know. In patients who are past or current smokers, baricitinib should only be used if no suitable treatment alternatives are available*. A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 84.7% [79.6%-88.9%]) over dermatologists (correct response rate 70.6% [65.4%-75.4%]).

Question 16b: *Please answer True or False [correct response] or I don't know. For patients with depression a 2 mg once daily dose is recommended*. A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 81.5% [76.0%-86.1%]) over dermatologists (correct response rate 68.2% [62.9%-73.1%]).

Question 17a: *Please answer True [correct response] or False or I don't know. An increased incidence of major adverse cardiovascular events have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors*. A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 85.9% [80.9%-90.0%]) over dermatologists (correct response rate 74.8% [69.8%-79.4%]).

Question 17c: *Please answer True [correct response] or False or I don't know. An increased incidence of serious infections have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors*. A difference was noted by prescriber specialty favouring dermatologists (correct response rate 39.6% [34.3%-45.1%]) over rheumatologists (correct response rate 17.7% [13.2%-23.1%]).

Question 18: *Which of the following statements is correct? (Please select one option). Response: Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy*. A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 68.5% [62.4%-74.3%]) over dermatologists (correct response rate 53.2% [47.6%-58.6%]).

By prescribing status (KRMs)

When stratifying participants' responses by prescribing status, differences (based on non-overlapping CIs) between responses of were noted for the following KRMs (Source Table 4.2):

KRM#2 Lipid parameters (Q9): A difference was noted by prescribing status favouring active prescribers (correct response rate 92.4% [89.7%-94.5%]) over potential prescribers (correct response rate 75.8% [65.9%-84.0%]).

KRM#3 Infections (Q10, Q11, Q12): A difference was noted by prescribing status favouring active prescribers (correct response rate 75.7% [71.7%-79.5%]) over potential prescribers (correct response rate 61.1% [50.5%-70.9%]).

KRM#7 Dosing (Q16a, Q16b, Q16c): A difference was noted by prescribing status favouring active prescribers (correct response rate 54.5% [50.0%-59.0%]) over potential prescribers (correct response rate 37.9% [28.1%-48.4%]).

By prescriber specialty (KRMs)

When stratifying participants' responses by specialty, differences (based on non-overlapping CIs) between responses were noted for the following KRMs (Source Table 4.3):

KRM#2 Lipid parameters (Q9): A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 94.0% [90.2%-96.6%]) over dermatologists (correct response rate 86.5% [82.3%-90.0%]).

KRM#5 MACE (Q14a, Q14b, Q14c): A difference was noted by prescriber specialty favouring rheumatologists (correct response rate 54.8% [48.4%-61.1%]) over dermatologists (correct response rate 41.7% [36.4%-42.7%]).

No differences were noted among the subgroups based on prescribing frequency or prescriber experience. In addition, no difference in any of the subgroup analyses were noted for understanding of the Objective 1 KRMs by country, by specialty, by prescribing frequency, or prescriber experience or the Objective 2 KRMs by any subgroup.

10.4.1. Communication of Important Safety Information

Subgroup analysis of responses to questions about the communication of important safety information to patients prescribed baricitinib showing stratification of participants' responses by country of practice, prescribing status, prescriber specialty, prescribing frequency, and prescriber experience are described in Section 9.9.4, and the full set of tables are provided in Annex 1, Appendix 1.2. These analyses were descriptive in nature. No CIs or statistical tests were used to assess differences between subgroups.

10.4.2. Distribution of the Patient Alert Card

Subgroup analysis of responses to questions about the PAC for baricitinib showing stratification of participants' responses by country of practice, prescribing status, prescriber specialty, prescribing frequency, and prescriber experience are described in Section 9.9.4, and the full set of tables are provided in Annex 1, Appendix 1.2. These analyses were descriptive in nature. No CIs or statistical tests were used to assess differences between subgroups.

10.5. Sensitivity Analyses

A post-hoc sensitivity analysis was completed to assess the results of the extra dermatology respondents from Germany. Per the protocol, a maximum number of 80 completed surveys by either rheumatologists or dermatologists was to be accepted from each country to maximise the generalisability of the survey results. Of the 581 respondents who completed the survey, 74 were from Sweden (28 rheumatologists; 46 dermatologists), 153 were from France (81 rheumatologists; 72 dermatologists), 211 from Germany (80 rheumatologists; 131 dermatologists), and 143 were from Spain (59 rheumatologists; 84 dermatologists). A post-hoc analysis including all the responses from the 81st to the 131st dermatology respondents in Germany indicated there was no change in understanding each of the KRMs (Table 3.1 vs Table 3.1A in Appendix 1.2); therefore, the inclusion of 51 respondents more than allowed by protocol did not alter the results.

10.6. Adverse Events and Product Complaints

Adverse event and product complaint information were not collected during this survey. In addition, no reports were collected spontaneously during communications with HCPs.

11. Discussion

11.1. Key Results

A total of 530 HCPs contributed to the main analysis, this included 282 dermatologists and 248 rheumatologists. Many (83.4%) of the HCPs had previously prescribed baricitinib; half (50.5%) of which had treated 1 to 5 patients with baricitinib in the previous 6 months and 46.4% treated 6 or more patients in the last 6 months. There was a rather stable distribution of years experience across the HCPs. This descriptive information provides an understanding that respondents to this survey were mostly familiar with baricitinib, spanned a length of professional experience, and ranged from light to more frequent prescribing of baricitinib.

11.1.1. Objective 1

The first objective of this observational study was to assess the effectiveness of the updated baricitinib HCP Educational Materials and PAC among dermatologists and rheumatologists. The KRMs within these materials included those pertaining to:

- KRM#1: Pregnancy (Q8)
- KRM#2: Lipid parameters (Q9)
- KRM#3: Infections (Q10, Q11, Q12)
- KRM#4: VTE (Q13a, Q13b, and Q13c).
- KRM#5: MACE (Q14a, Q14b, and Q14c)
- KRM#6: Lymphoma and other Malignancies (Q15a, Q15b).
- KRM#7: Dosing (Q16a, Q16b, and Q16c).

The initial iteration of this study included KRMs 1 through 4. The risk messages pertaining to MACE, malignancies, and dosing (KRM5 through 8) were added as a result of the changes in the aRMMs at the conclusion of the Article 20 referral.

11.1.1.1. Response to individual questions:

With the exception of one question pertaining to Objective 1, all were answered correctly by at least 71% of rheumatologists/dermatologists who completed the survey.

Individual questions (Q9, Q10, Q11) and items of questions (all 3 items of Question 13; 1 of 3 items of Question 14; 1 of 2 items of Question 15; and 2 of 3 items of Question 16) all had responses greater than 80% (Table 10.5. Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys).

The only question for which the response was less than 71% was for Question 14b, where only 66.8% of respondents correctly identified that the statement, “Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors,” was false. This result should be put into context with the other two questions on the cardiovascular risk topic where 91.5% correctly identified that there is a potential increased risk of MACE in patients with certain risk factors using JAK inhibitor treatment including baricitinib and 77.2% correctly identified that in patients who are past or current smokers, baricitinib should only be used if no suitable alternatives are available.

11.1.1.2. Responses to KRMs:

To be counted as demonstrating understanding of a specific KRM, respondents were required to answer all questions/items of the KRM correctly. Respondents' demonstrated understanding of the risk messages pertaining to Objective 1 were as follows:

- KRM#1 Pregnancy (Q8), 73.0%
- KRM#2 Lipid parameters (Q9), 90.4%
- KRM#3 Infections (Q10, Q11, Q12), 73.4%
- KRM#4 VTE (Q13a-c), 81.9%
- KRM#5 MACE (Q14a-c), 47.9%
- KRM#6 Lymphoma and other malignancies (Q15a-b), 66.0%, and
- KRM#7 Dosing (Q16a-c), 52.8%

The proportion of responding HCPs that correctly answered all 16 items contributing to the 7 KRMs for Objective 1 was 14.3%.

Regarding KRMs 1 through 3 on pregnancy, lipids, and infections, the demonstrated understanding of these specific KRMs in this study were consistent with results from the non-interventional post authorisation safety study (PASS) survey of baricitinib RMMs conducted among 226 rheumatologists in Germany, Sweden, UK, and France (Study I4V-MC-B010, 2020). Study 14V-MC-B010 assessed only understanding of the educational materials related to pregnancy and breastfeeding, infections, reactivation of viral infections and changes in lipid parameters. HCP overall understanding was similar for pregnancy and breastfeeding (72.6%); lipid parameters (91.2%); and, management of infections (79.2%) and, reactivation of viral infections was 72.1%.

Regarding KRM #4 on VTE, this understanding was strong with 81.9% of respondents understanding all 3 elements of the risk message.

The newest risk messages within the aRMM are KRMs #5 through #7 on MACE, malignancy, and dosing. Understanding of these risk messages was slightly lower than the longer standing risk messages of the aRMM at 47.9%, 66.0%, and 52.8%, respectively. While only 47.9% of respondents understood all 3 elements of the MACE risk message, as discussed earlier, this overall percentage was largely driven by HCP over assessing the risk and inappropriately assessing a contraindication among patients with increased cardiovascular risk. And the individual questions within the malignancy and dosing KRMs all scored above 73%.

11.1.2. Objective 2

The second objective of this observational study was to assess the effectiveness of a DHPC distributed to rheumatologists and dermatologists. It should be noted that the development of the DHPC was at the request of the PRAC following an Article 20 referral. The letter was developed jointly by the 4 EU MAHs of the 5 EU-approved JAK inhibitors and was not specific to baricitinib. While this study included an objective to assess the effectiveness of the letter to communicate the class-wide risk, it should be noted that current Good Pharmacovigilance Practices (GVP) Module XVI Rev 3 came into effect after the development of this protocol

(Head of Medicines Agency [HMA] and EMA, 2024). GVP Module XVI Rev 3 describes DHPC letters as a safety communication tool to support dissemination of the aRMM. Thus, they are not themselves aRMM that require effectiveness assessment under current guidelines.

The relevant questions to address Objective 2 were based on 1 KRM regarding the JAK inhibitor class effects (Q17a, Q17b, Q17c, Q17d, Q18, Q19).

For objective 2, more than 80% of respondents answered correctly to Question 17a and 17b which required an answer of true to the question as to whether there was an increased incidence of MACE and VTE observed with JAK inhibitor treatment compared to TNFα inhibitors. 78.3% responded correctly that periodic skin examination is recommended for patients treated with baricitinib. This suggests that there is a good understanding of the cardiovascular and thromboembolic risks associated with JAK inhibitors and a good understanding of the recommended medical practice to assess the patient for skin cancer.

For objective 2, there was a much lower percentage of correct responses for questions comparing JAK inhibitors with TNFα inhibitors with respect to serious infections (29.2%), mortality (18.5%) and malignancy (60.6%). A possible explanation for this is that these events are also associated with TNFα inhibitor treatment and respondents may not have known whether the incidence was higher or lower for JAK inhibitors. This theory is supported by the responses for Objective 1 where 95.7%, 94.7%, and 78.3% of respondents correctly answered the three questions concerning the infection risk specific to baricitinib and 71.7% and 88.3% of respondents correctly answered the two questions regarding the malignancy risk specific to baricitinib.

For Objective 2, the proportion of respondents that demonstrated understanding of the single KRM pertaining to Objective 2 by answering all 6 questions correctly was:

- JAK inhibitor class effect (Q17a-d, Q18, Q19), 7.5%

11.1.3. Subgroup Analyses

As described in the methods (Section 9.9.4), responses to individual questions and KRMs were analysed according to pre-specified subgroups including by country, speciality (rheumatologist/dermatologist), whether they are active prescribers of baricitinib, among other prescriber characteristics. Differences were noted in subgroup analyses for overall understanding of the KRMs and select individual questions and items of questions based on non-overlapping CIs (Section 10.4).

Differences by country were noted for individual questions related to the understanding of important safety information (Q12, Q14c, Q16a, and Q16c), however, no clear pattern emerged for one country responding consistently better overall than another as most responses by country were at least 70% or higher (Source Table 3.1).

Subgroup analyses by specialty are of particular interest given the more recent approval of baricitinib for dermatology indications and the differences in baseline risk of events between rheumatology and dermatology patients. Study B010 established effective aRMM

communication for select risk messages for rheumatologists (Study I4V-MC-B010, 2020). This current study is the first assessment of aRMM effectiveness among dermatologists. Understanding was overall high in both rheumatologists and dermatologists; however, differences by prescriber specialty were noted for individual questions related to the understanding of important safety information (Source Table 3.3). However, the select questions with differences by speciality (Q9, Q11, Q14c, Q16b, Q17a, Q17c, and Q18) are re-presented below in Table 11.1. Subgroup Results by Specialty for Select Individual Questions Where Differences Were Noted Based on Non-overlapping Confidence Intervals for ease of discussion. Most responses to individual questions by prescriber specialty were at least 70% or higher and differences in scores favouring rheumatologists ranged from 3.5% to 15.3% across 5 of 6 questions; for Q17c, the difference in score favouring dermatologists was 21.9%) (Source Table 3.3).

Table 11.1. Subgroup Results by Specialty for Select Individual Questions Where Differences Were Noted Based on Non-overlapping Confidence Intervals

	Rheumatologists (N=248) n (%) [95% CI]	**Dermatologists (N=333) n (%) [95% CI]**
Q9: Which of the following statements is correct? (correct answer) *In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected.*	233 (94.0) [90.2-96.6]	288 (86.5) [82.3-90.0]
Q11: Which of the following statements is correct? (correct answer) *Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy.*	243 (98.0) [95.4-99.3]	308 (92.5) [89.1-95.1]
Q14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available.	210 (84.7) [79.6-88.9]	235 (70.6) [65.4-75.4]
Q16b: For which patients is a 2 mg once daily dose recommended. Please answer True, False, or I do not know. *Patients with depression.* (Correct answer was "False")	202 (81.5) [76.0-86.1]	227 (68.2) [62.9-73.1]
Q17a: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know. *MACE* (correct answer was true)	213 (85.9) [80.9-90.0]	249 (74.8) [69.8-79.4]
Q17c: *Serious infections* (correct answer was true)	44 (17.7) [13.2-23.1]	132 (39.6) [34.3-45.1]
Q18: Which of the following statements is correct? (correct answer) *Compared with TNFα, JAK inhibitor treatment has been associated with an increased incidence of malignancy*	170 (68.5) [62.4-74.3]	177 (53.2) [47.6-58.6]

Source: Table 3.3

A similar pattern was seen in the subgroup analysis of each KRM for Objective 1 by specialty. Rheumatologists performed better than dermatologists for KRM #2 Lipid parameters (94.0% versus 86.5%), and KRM #5 MACE (54.8% versus 41.7%). This may be a reflection on the fact that baricitinib has been approved for RA for longer than for AD and hence HCPs are more familiar with the safety concerns (Source Table 4.3). However, whilst this would explain why rheumatologists scored higher than dermatologists for the KRM which were included in the original educational materials (pregnancy and lactation, infection, changes in lipid parameters), it does not explain why they scored higher regarding the major cardiovascular event risk as this was only the subject of the revised educational materials by which time baricitinib was also approved for AD.

Differences by prescriber status were noted for individual questions related to the understanding of important safety information (Q9, Q14c, Q16a, Q16b, and Q16c) with active prescribers performing better than potential prescribers. Most responses by prescriber status were at least 70% and differences in scores favouring active versus potential prescribers ranged from 14% to 19.9% across the 5 questions) (Source Table 3.2). A similar pattern was seen in the subgroup analysis of each KRM for Objective 1 by prescribing status (instead of by the individual questions). Active prescribers performed better than potential prescribers for KRM #2 Lipid parameters (92.4% versus 75.8%), KRM #3 Infections (75.7% versus 61.1%) , and KRM #7 Dosing (54.5% versus 37.9%).This is to be expected as those HCPs who actively prescribe are more likely to consider the safety information than those who have never prescribed, even if they may potentially do so in the future (Source Table 4.2).

Overall for the remaining subgroup analyses, no differences were noted in response rates to questions stratified by prescribing frequency or prescriber experience.

In the post-hoc sensitivity analysis conducted including all German respondents to determine if the results from the additional respondents had any effect on the results of this survey, the analysis resulted in no difference in results.

11.1.4. Awareness of aRMM and Communication of Important Safety Information

In addition to the questions pertaining to the HCPs knowledge of risks, the survey included questions to understand awareness of the aRMM and behaviours around communicating risks.

- HCP Educational Material awareness: Slightly more than half of all respondents (52.1%) indicated they were aware of the HCP educational materials. Of these 60.9% reported that they had received a copy of the materials. Of those that reported to have received a copy, 75.6% reported that they had read the materials.
- PAC awareness: Similarly, 52.3% indicated they were aware of the PAC for baricitinib. Of these 8.5% indicated that when prescribing baricitinib for the first time their patient is provided with a PAC. Among 190 respondents who indicated they had both prescribed baricitinib and were previously unaware of the PAC (thus could not have provided it at first prescription), 92.6% indicated that someone in their practice/hospital communicates the important information to their patients when prescribing baricitinib for the first time.

- DHPC letter awareness: About 2/3 of respondents (69.1%) indicated they had received a copy of the DHPC. Of those who reported to have received it, 88.8% respondents indicated that they had read it.

The high level of knowledge of the safety information in the KRM demonstrated in Objective 1 results, combined with the relatively low number of respondents who were aware of and read the aRMM, suggests that either the respondents did not recall accurately the receipt of the materials or that HCPs obtained safety information from other sources in addition to the HCP Educational Materials.

It is worth noting that the PACs are also distributed directly to the patient, as they are attached to the PIL which is provided with every package of baricitinib.

11.2. Limitations

The database of dermatologists and rheumatologists in each country from which the recruitment mailing list was derived was a database of prescribers who had previously agreed to participate in survey research. This approach of only contacting HCPs who had consented to be contacted for research purposes has been taken to be compliant with the General Data Protection Regulation (GDPR, 2018). However, there was possible selection bias by not reaching out broadly to all practicing rheumatologists or dermatologists in each of the 4 countries. The difficulties of survey research in the EU because of data protection regulations and possible selection bias issues were highlighted in a White Paper by the International Society for Pharmacoepidemiology on Measuring the Impact of Pharmacovigilance Activities (Madison, 2016).

Participants who agreed to be included in this type of research database may differ in their knowledge and prescribing characteristics from the overall group of practicing clinicians in each country. Given the restrictions of the GDPR that individuals may only be contacted if they have agreed to the contact, it was not possible to contact all HCPs that receive the aRMM materials. Therefore, this type of selection bias is a possibility for all survey-based research where the participants who do respond to the survey may differ from those who do not respond.

The survey recruitment strategies are intended to recruit dermatologists and rheumatologists who report that they are prescribers or potential prescribers of baricitinib. Participants were self-selected since they voluntarily responded to the invitation to participate, so the potential exists that those who choose to respond to the survey may differ in their understanding of the important safety information from those who elect not to participate.

This is a common limitation of all studies that rely on voluntary participation. In order to address this potential selection bias a limited non-respondent survey was included and was offered to those who decline to respond to the full survey. Subjects who decline to participate were nonetheless able to elect to respond to 2 questions aimed at understanding whether they differ in important ways from those who volunteer to respond to the survey. Specifically, these questions requested information on whether non- respondents have prescribed baricitinib (Q1a) and whether they are aware of the important safety information communicated in the HCP

Educational Materials and in the DHPC communication (Q1b). However, there were very few potential participants who did not agree to take part in the survey. Of those who did not agree to take part, they discontinued without answering these two questions.

Among those who volunteer to respond to the survey, recall of information was critical. Inherent in survey research is the reliance on the respondent's recall of whether or not the documents were received. If the respondent says she/he did not receive them, the risk minimisation programme is evaluated as not optimally disseminating the materials. It is possible, however, that respondents may simply not recall receiving these documents even thought they were, in fact, received.

It is also possible that the respondents have acceptable understanding of the important safety information despite not receiving or recalling receipt of the documents. The survey can assess the participants' understanding of the important safety information but cannot clearly determine via which channel they gained the information.

All data from the survey were self-reported and therefore susceptible to possible reporting bias in that respondents may select the socially desirable response rather than the true response. This may be particularly true for the questions regarding the receipt and reading of the DHPC.

11.3. Interpretation

The present study achieved its key objectives through the successful attainment of its target sample size and recruitment of participants who were diverse with respect to their geographic region, duration of practice within their specialty, and experience with the treatment of patients with baricitinib.

The objectives of this study were to assess the effectiveness of the updated baricitinib HCP Educational Materials, PAC, and DHPC distributed among dermatologists and rheumatologists. Overall results indicate that 14.3% and 7.5% of HCPs demonstrated an understanding of all KRMs that constituted the first and second objective, respectively. While these appear to be relatively small frequencies, these figures represent those who answered all questions associated with each KRM correctly. Therefore, further consideration of individual questions that comprise each KRM is instructive and can aid in contextualising these more restrictive estimates. From this perspective, 15 of the 16 questions that constituted the KRMs of objective 1 are above 71%. These results were aligned with a prior non-interventional PASS study (I4V-MC-B010, 2020), which assessed understanding of the educational materials related to pregnancy and breastfeeding, infections, reactivation of viral infections and changes in lipid parameters. Additionally, 3 of the 6 questions constituting KRM #8 of Objective 2 were above 78%.

Variability in the results observed between KRM's could be partly explained by several factors. First, respondents' understanding of some KRM's are evaluated with one question, whereas others are evaluated with multiple questions. Although not absolute, KRM's assessed with multiple questions (e.g., cardiovascular events and dosing) tended to exhibit lower levels of understanding by providers, which may simply reflect the more restrictive conditionality imposed by answering multiple questions correctly vs. one. Second, an appreciable number of

prescribers' responses that were classified as "incorrect," did in fact demonstrate a degree of understanding of the risks associated with baricitinib. For instance, in Question 14b, which asked participants whether baricitinib is contraindicated in patients with cardiovascular risk factors, many respondents chose "TRUE." While incorrect, this selection does suggest that providers are aware of cardiovascular risks associated with the medicine and contextualises the challenges respondents faced in answering multiple questions correctly across each KRM. Also, this imprecise understanding would not place patients at risk as assuming a contraindication in this case is more conservative from a patient safety standpoint.

While this study is descriptive and there were no pre-specified criteria for demonstrating effectiveness of aRMM, the results suggest that practicing dermatologists and rheumatologists are largely aware of the communicated risks of baricitinib.

11.4. Generalisability

This HCP survey took place across four EU countries where baricitinib is marketed for the indications of RA, AD, and AA. In order to ensure there was equal spread across the four countries and to maximise generalisability, a limit of a maximum of 80 surveys for each speciality in each country was made. Recruitment into the survey was rapid and as a result, more than 80 surveys from dermatologists in Germany were obtained. Whilst the primary analysis included only the first 80 German dermatologists, a post-hoc analysis including all the responses from the 81st to the 131st dermatology respondents in Germany indicated there was no change in understanding each of the KRMs.

Overall 76.4% of respondents were prescribers of baricitinib indicating that the survey was representative of prescribers.

12. Other Information

Not applicable.

13. Conclusions

The results of this survey showed that:

- 15 of the 16 individual questions pertaining to KRMs of baricitinib were correctly answered by at least 71% of HCPs:
    - Understanding was highest for the overall risk messages around need to monitor lipids and risk of VTE. Understanding was lowest for risk messages around risk of MACE and dosing.
- Subgroup analyses according to specialty were generally consistent with slightly better understanding of safety messages among rheumatologists than dermatologists.
- Awareness of the specific aRMM (i.e., the HCP Education Material and the PAC) was modest with 52% of HCPs aware of each. Despite low awareness of the HCP Educational Material, knowledge of risks was high. Despite low awareness of the PAC, 92.6% of HCPs that are unaware of the PAC and prescribe baricitinib communicate risk information at first prescription.
- 69.1% of respondents indicated they received a copy of the DHPC, and 88.8% of those respondents indicated reading it. Given that the distribution of the DHPC is complete, risk messages for baricitinib are understood based on Objective 1, and consistent with GVP Module XVI Rev 3, the DHPC can be removed from the baricitinib EU RMP as an aRMM activity.

The results of this study support that both rheumatologists and dermatologists have good understanding of the risks associated with baricitinib. This is consistent with a previous survey assessment of baricitinib aRMM effectiveness for rheumatologists and for the first time provides evidence that dermatologists also understand the safety information for baricitinib. This understanding of risks is likely resulting from a combination of risk minimisation activities including routine (Summary of Product Characteristics) and additional activities (such as the aRMM).

Based upon this current evaluation of the knowledge, understanding and behaviours, the aRMM were determined effective. No changes to the ongoing aRMM are warranted based on the results of this study.

14. References

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Annex 1. List of Standalone Documents

No.	Document Reference No.	Date	Title
1.	Appendix 1.1	01 March 2024	Protocol Amendment c: Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant® (baricitinib) a JAK1/2 inhibitor.
2.	Appendix 1.2		Final Tables and Listings

Appendix 1.1: PROTOCOL Amendment c, 01 March 2024

Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant (baricitinib), a JAK1/2 Inhibitor

Study I4V-MC-B025

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Protocol Electronically Signed and Approved by Lilly: 20 October 2021
Amendment (a) Electronically Signed and Approved by Lilly: 21 April 2023
Amendment (b) Electronically Signed and Approved by Lilly: 13 September 2023
Amendment (c) Electronically Signed and Approved by Lilly: approval date provided below

Document ID: VV-PVG-112157

Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant (baricitinib), a JAK1/2 Inhibitor

PASS Information

Title:	Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant® (baricitinib) a JAK1/2 inhibitor
Study Identifier	I4V-MC-B025
Version identifier:	Amendment c
Date of last version:	Amendment b: 13 September 2023 Amendment a: 21 April 2023 Original protocol: 20 October 2021
European Union (EU) Post Authorisation Study (PAS) Register No:	EUPAS43239
Active substance:	Baricitinib ATC Code: L04AA37
Medicinal product(s):	Baricitinib
Product reference:	EMEA/H/C/004085
Procedure number:	To be added after submission
Marketing authorisation holder(s) (MAH):	Eli Lilly Nederland B.V.
Joint PASS:	Not Applicable (N/A)
Research question and objectives:	This study will assess: 1. The effectiveness of the updated baricitinib healthcare professional (HCP) Educational Materials and Patient Alert Card (PAC) among dermatologists and rheumatologists 2. The effectiveness of a Direct Healthcare Professional Communication (DHPC) distributed to dermatologists and rheumatologists
Countries of study:	At least 3 EU countries: Sweden, France and Germany.

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Approved on 01 Mar 2024 GMT

2. List of Abbreviations

Term	Definition
aDCT	Annotated Data Collection Tool
AA	alopecia areata
AD	atopic dermatitis
aRMM	additional risk minimisation measure
ATC	Anatomical Therapeutic Chemical
B025	Study I4V-MC-B025
CFR	Code of Federal Regulations
CHMP	Committee for Medicinal Products for Human Use
CIOMS	Council for International Organisations of Medical Sciences
CI	confidence interval
DHPC	Direct Healthcare Professional Communication
EDC	electronic data capture
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EU	European Union
EULAR	European League Against Rheumatism
FDA	United States Food and Drug Administration
GDPR	General Data Protection Regulation
GEP	Good Epidemiological Practice
GPP	Good Pharmacoepidemiology Practices
GVP	Good Pharmacovigilance Practices
HCP	healthcare professional
ICD	International Classification of Disease
ICH	International Council for Harmonisation
IEA	International Epidemiological Association
ISPE	International Society for Pharmacoepidemiology
IT	Information Technology
JAK	Janus kinase
JAKi	Janus kinase inhibitor
KRM	Key Risk Message
Lilly	Eli Lilly and Company
MACE	major adverse cardiovascular event
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
N/A	not applicable
NCA	National Competent Authority
NMSC	non-melanoma skin cancer
PAC	Patient Alert Card
PAS	post authorisation study
PASS	post authorisation safety study
PRAC	Pharmacovigilance and Risk Assessment Committee

RA	rheumatoid arthritis
RMM	risk minimisation measures
RMP	Risk Management Plan
SAR	suspected adverse reaction
SAS	Statistical Analysis Software
SDLC	System Development Life Cycle
SmPC	Summary of Product Characteristics
SOPs	Standard Operating Procedures
SSRS	Server Reporting Services
TLFs	tables, listings, and figures
TNFα	Tumour Necrosis Factor alpha
TNFi	Tumour Necrosis Factor inhibitor
UBC	United BioSource LLC
UK	United Kingdom
USA	United States of America
VTE	venous thromboembolism
WHO	World Health Organisation

3. Responsible Parties

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4. Abstract

Title: Rheumatologist and Dermatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant® (baricitinib) a JAK1/2 inhibitor.

Rationale and Background:

Baricitinib is a Janus kinase (JAK) 1/JAK2 inhibitor that was first approved for the treatment of rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs. When baricitinib was first authorised for use in the European Union (EU) in February 2017, additional risk minimisation activities were included as part of the EU Risk Management Plan (RMP). These activities include:

(i) the Healthcare Professional (HCP) Educational Materials to inform the initial discussion between the rheumatologist and patient at time of first prescribing about important safety information related to the use of baricitinib during pregnancy or breastfeeding, the potential risk of infection, and changes in lipid parameters associated with the administration of baricitinib, and

(ii) a Patient Alert Card (PAC) with the same important safety information described above.

Additionally, Lilly committed to conduct of a survey of rheumatologists to assess the effectiveness of the above listed risk minimisation activities (Study I4V-MC-B010). The survey was designed to assess rheumatologists' understanding of the important safety information detailed in the HCP Education Materials and assess the communication of the important safety information and distribution of the PAC to patients prescribed baricitinib for the first time.

Subsequently, baricitinib has been approved for the indication of moderate to severe atopic dermatitis (AD) in adult patients who are candidates for systemic therapy and for the treatment of severe alopecia areata (AA) in adult patients.

Additionally, the HCP Educational Materials and the PAC for all indications have been updated to include important safety information on venous thromboembolism (VTE), major adverse cardiovascular events (MACE), lymphoma and other malignancies and dosing recommendations.

Also, a Direct Healthcare Professional Communication (DHPC) has been distributed to dermatologists and rheumatologists to draw attention to the increased incidence of MACE, serious infections, VTE and mortality seen with JAK inhibitor treatment.

Research Questions and Objectives: This study will assess the following:

1. The effectiveness of the updated baricitinib HCP Educational Materials and PAC among dermatologists and rheumatologists
2. The effectiveness of a DHPC distributed to dermatologists and rheumatologists

- **Study Design:** This study uses a multi-national, observational cross-sectional design. Approximately 400 completed surveys will be obtained with approximately 200 from dermatologists and 200 from rheumatologists. No more than 80 completed dermatology surveys and 80 completed rheumatology surveys will be accepted from any individual country.
- **Population:** The survey will be administered to dermatologists and rheumatologists in at least 3 EU countries: Sweden, France and Germany. The targeted respondent population will be dermatologists of whom at least 50% will have prescribed baricitinib and rheumatologists of whom at least 50% will have prescribed baricitinib.

  Screening questions will be used to determine respondent eligibility for the survey. Individuals who have ever worked directly for, or whose immediate family members have ever worked directly for Eli Lilly and Company (Lilly) or any of its affiliates, United BioSource LLC (UBC), IQVIA, the European Medicines Agency (EMA) or any National Competent Authority (NCA) will not be considered for participation.

- **Study Endpoints**: For Objective 1, the study endpoints are the correct understanding of each Key Risk Message (KRM) (Questions 8-16 pertaining to pregnancy, lipid changes, infections and VTE, MACE, lymphoma, and other malignancies and dosing as communicated in the HCP Educational Materials).

  The survey will also assess whether HCPs (a) communicate the important safety information and mitigating actions to patients prescribed baricitinib for the first time, and (b) distribute the PAC to patients prescribed baricitinib for the first time.

  For Objective 2, the study endpoints are the correct understanding of each KRM (Questions 17-19) pertaining to the JAK inhibitor class effects communicated in the DHPC.

- **Variables:** The survey will collect responses to each question required to address the study objectives, in addition to prescriber status (yes/no), demographic information (e.g., country of practice), and clinical experience (e.g., duration of experience treating patients with relevant indication, number of patients for whom they have prescribed baricitinib).

- **Data Sources**: Structured, self-administered surveys comprising closed-ended questions or statements with multiple-choice responses will be used to collect the data.

- **Study Size**: The study will target completion of approximately 400 surveys (approximately 200 dermatologists and approximately 200 rheumatologists), with at least 50% of those from dermatologists who have prescribed baricitinib and 50% from rheumatologists who have prescribed baricitinib. This will provide an estimated precision of ±7% around the observed proportion of correct responses (for each speciality) who answer correctly, assuming the true proportion is 50%. If the true proportion is greater or lesser than 50%, the estimated proportion will be more precise. The maximum number of completed surveys from any individual country will be set to 80 dermatologists and 80 rheumatologists.

- **Data Analysis:** Data collected from the survey will be reported using descriptive statistics. In addition to the overall analysis of the survey data collected, data will also be analysed by country, by speciality (dermatologist or rheumatologist) and prescriber status (has previously prescribed baricitinib [i.e., prescriber], has not previously prescribed baricitinib [i.e., potential prescriber]), by number of patients treated, and by

clinical experience. Responses to each question relating to the understanding of risks will be categorised as "Correct" or "Incorrect". Frequency distributions with 95% confidence intervals (CIs) will be calculated for responses to questions that address the survey objective (excluding demographic questions).

- **Milestones:** Data collection will commence within 3 months after both the DHPC and updated risk minimisation materials have been distributed in each participating country and a positive Committee for Medicinal Products for Human Use (CHMP) opinion on the protocol has been received. Data collection is estimated to start by 31 October 2023 and end when 400 surveys have been completed which is estimated to be 31 October 2024. Findings from the survey results will be reported to regulatory authorities (Section 6) with the study report expected by 30 April 2025.

5. Amendments and Updates

Amendment or Update Identifier	Date	Section of Study Protocol	Amendment or Update	Reason
a	21 April 2023	Title 8. Research Question and Objectives 9. Research Methods Appendix I.1 Survey	Inclusion of Rheumatologists in addition to Dermatologists Total study size increased to 400 participants Changes to Survey questions to test revised KRMs in HCP educational materials and DHCP Communication	Objectives and Survey Target Population expanded consistent with commitment made in the Article 20 referral
		Cover page 9. Research Methods Appendix I.1 Survey	Country change: Belgium replaced by Sweden	Feasibility to perform study
b	13 September 2023	9.7 Data Analysis 9.9 Limitations of the Research Methods	Removal of the target success threshold	Per PRAC review of protocol: Threshold is arbitrary and may not give full justice to study results and limit their interpretation
		9.9 Limitations of the Research Methods	Added limitation of recruitment method	Clarification of survey recruitment methods and how this is related to selection bias
		9.4 Data Sources	Revised methods for target sample size determination to ensure representativeness	Clarification of target sample size
		9.3 Variables 9.7 Data Analysis Survey Questionnaire	Removed Question 8 from survey	Per PRAC review of protocol: Age is not required as a confounder or stratification variable
c	See cover page	9.2 Setting 9.4 Data sources 9.6 Data management 9.9.1 Controls to minimise bias	Deleted telephone survey option and added technical support via telephone option	Change in capabilities within the vendor executing studies

Amendment or Update Identifier	Date	Section of Study Protocol	Amendment or Update	Reason
		Appendix I.1 Proposed Survey (online survey and paper survey) Appendix I.2 Sample Draft Survey Invitation Letter		

6. Milestones

Milestone	Planned* Timeline
Submission of protocol	**25 April 2023**
Start of data collection	**Within 3 months after both the DHPC and updated risk minimisation materials have been distributed in each participating country and a positive CHMP opinion of the protocol.** **Estimated by 31 October 2023**
End of data collection	**When at least 400 surveys have been completed (200 dermatologists and 200 rheumatologists), estimated at 31 October 2024**
Registration in the EU PAS Register	**Prior to start of data collection**
Final study report	**6 months after the end of data collection, estimated 30 April 2025**

*The proposed start date for the survey depends on the timing of the CHMP opinion of the protocol (based on EMA timetable for Post Authorisation Measure assessment) as well as the DHPC distribution and implementation of updated risk minimisation materials (i.e., the PAC and HCP Educational materials) in each participating country.

7. Rationale and Background

Baricitinib is a Janus kinase (JAK) 1/JAK2 inhibitor that was first approved for the treatment of rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs. When baricitinib was first authorised for use in the European Union (EU) in February 2017, additional risk minimisation activities were included as part of the EU Risk Management Plan (RMP). These activities included:

(i) the Healthcare Professional (HCP) Educational Materials to inform the initial discussion between the rheumatologist and patient at time of first prescribing about important safety information related to the use of baricitinib during pregnancy or breastfeeding, the potential risk of infection, and changes in lipid parameters associated with the administration of baricitinib, and

(ii) a Patient Alert Card (PAC) with the same important safety information described above.

Eli Lilly and Company (Lilly) conducted a survey of rheumatologists to assess the effectiveness of the above listed risk minimisation activities. The survey was designed to assess rheumatologists' understanding of the important safety information detailed in the HCP education materials and assess the communication of the important safety information and distribution of the PAC to patients prescribed baricitinib for the first time. The final study report for Study B010 concluded that the risk minimisation materials were effective; rheumatologists understood the safety information for baricitinib and communicated these messages to their patients (Procedure EMEA/H/C/004085/II/0017 with Committee for Medicinal Products for Human Use [CHMP] positive opinion 29 October 2020).

Subsequently, baricitinib was approved for the indication of moderate to severe atopic dermatitis (AD) in adult patients who are candidates for systemic therapy in October 2020 and for the treatment of severe alopecia areata (AA) in adult patients in June 2022. With the expansion of marketing authorisation into dermatologic conditions, Lilly originally committed to survey dermatologists to ensure the risk minimisation materials were also effective among dermatologists (Study I4V-MC-B025; committed to in EU RMP v8.1 [Procedure EMEA/H/C/004085/II/0016]).

Implementation of Study B025 was held as part of a safety variation submitted to the Pharmacovigilance and Risk Assessment Committee (PRAC) by Lilly 29 October 2021, and then by the Article 20 referral for Janus kinase inhibitors (JAKi) (10 February 2022). With the completion of the Article 20 referral (10 March 2023), the scope of B025 was expanded to include rheumatologists as well as dermatologists, and to assess the resulting Risk Minimisation Measures (RMMs) which included updated educational materials and a Direct Healthcare Professional Communication (DHPC). The HCP Educational Materials and the PAC for all indications were updated to include additional important safety information on venous thromboembolism (VTE), major adverse cardiovascular events (MACE), lymphoma and other malignancies and dosing recommendations.

The DHPC has been distributed to dermatologists and rheumatologists to communicate the increased incidence of MACE, serious infections, VTE and mortality seen with JAK inhibition treatment compared to Tumour Necrosis Factor inhibitors (TNFi).

8. Research Question and Objectives

This study will assess the following:

Research Questions and Objectives: This study will assess the following:

1. The effectiveness of the updated baricitinib HCP Educational Materials and PAC among dermatologists and rheumatologists. The key risk messages (KRMs) within these materials include those pertaining to:
    a. Pregnancy
    b. Infections
    c. Changes in lipid parameters
    d. VTE
    e. MACE
    f. Lymphoma and other malignancies
    g. Appropriate dosing
2. The effectiveness of a DHPC distributed to dermatologists and rheumatologists.

9. Research Methods

9.1. Study Design

This observational study is a multi-national cross-sectional survey.

9.2. Setting

Eligible dermatologists and rheumatologists from at least 3 EU countries (Sweden, France, and Germany) will be invited. These countries were chosen based upon sufficient market uptake of baricitinib to support target enrolment and sufficient numbers of dermatologists and rheumatologists who have indicated they are willing to participate in this type of research. The survey will be distributed within 3 months after both the DHPC and updated risk minimisation materials have been distributed in each participating country and a positive CHMP opinion of this protocol (see Section 6).

To maximize the generalisability of the survey results, a maximum number of completed surveys will be accepted from each country, so that no individual country is over-represented. No more than 80 completed surveys from each speciality will be accepted from any one country, i.e., a maximum of 80 dermatologists from each country and 80 rheumatologists from each country. Additional EU countries may be considered as necessary to meet target enrolment.

The HCP Educational Materials, the PAC and the DHPC will be sent to HCPs who are prescribers or potential prescribers of baricitinib in each country, as agreed by each National Competent Authority (NCA).

The target population in each selected country will be dermatologists and rheumatologists who have been sent the HCP Educational Materials, the PAC and the DHPC.

The same survey will be used for all participating countries to ensure consistency in testing the target population. As such, variability of survey results based on geography is not anticipated.

Respondents will have the option to complete the survey via the internet, which will allow respondents to participate at a time and location that is convenient for them. A dedicated telephone line will be available should respondents require technical support, encounter problems completing the survey online, or prefer a paper version of the survey.

9.2.1. Survey Target Population

The target populations for the survey are dermatologists and rheumatologists in the EU who have previously self-identified as being willing to receive invitations for survey research. At survey initiation, this will include dermatologists and rheumatologists in Sweden, France and Germany.

Inclusion criteria

Dermatologists or rheumatologists must meet the following criterion for inclusion in the survey:

- Must identify themselves as being previous prescribers or potential prescribers of baricitinib.

To ensure that survey results adequately reflect the knowledge of the main target of the survey; at least 50% of the total completed surveys for each speciality will be required from prescribers of baricitinib.

Exclusion criteria

Dermatologists or rheumatologists meeting the following criterion will not be permitted to take the survey:

- Current or past employment with Lilly or any of its affiliates, UBC, IQVIA, the European Medicines Agency (EMA) or any NCA.

9.3. Variables

The survey will collect responses to each question required to address the two study objectives:

Objective 1

- Response to questions about important safety information detailed in HCP Educational Materials, including key risk messages pertaining to:
    a. Pregnancy
    b. Infections
    c. Changes in lipid parameters
    d. VTE
    e. MACE
    f. Lymphoma and other malignancies
    g. Appropriate dosing
- Whether or not important safety information and mitigating actions to patients prescribed baricitinib for the first time was communicated, and
- Whether the PAC was distributed to patients prescribed baricitinib for the first time.

Objective 2

- Responses to questions about important safety events observed with JAKi as detailed in the DHPC letter.

In addition, information on the following will be collected:

- Speciality (rheumatologist/dermatologist)
- Prescriber status (yes, have previously prescribed/have not yet prescribed)
- Demographic information: geographic location (country), and
- Clinical experience: duration of experience treating patients with relevant indication (years), number of patients for whom they have prescribed baricitinib (count).

9.4. Data Sources

In order to target the desired population, the data source will be a database of dermatologists and rheumatologists sourced from IQVIA, a subcontractor of UBC, in each of the selected countries who have previously agreed to be contacted for this type of research. Based on feasibility assessments of the list of dermatologists and rheumatologists from each of the

participating countries, invitations will be sent to all rheumatologists in each country's list. There are larger numbers of dermatologists listed in Germany and France. Therefore, a 50% simple random sample will be selected and invited in each of these 2 countries while all dermatologists in Sweden will be invited.

Dermatologists and rheumatologists will receive an invitation letter via email and/or postal mail to participate in the survey. The invitation letter (Appendix I.2) will include: an overview of the rationale for the survey, information on how to access the survey online and telephone support in case of technical difficulties, and a unique invitation code to ensure that the invitation is used only once. Based on survey uptake within each respective country, reminder notices will be sent via email and/or postal mail to those who have been invited but have not yet participated. The database of invitees will be regularly updated with responders and after each invitation mailing, the database will be cross-checked with any correspondence that had an invalid address, was undeliverable or had incorrect contact details. Those who have been sent an invitation, and there is no evidence that it has not been received (e.g., an invalid address), and who do not respond within 2 weeks from the initial mailing, will receive at least 1 reminder invitation.

A structured questionnaire will be used to collect survey data (Appendix I.1). It is comprised of closed-ended questions or statements with multiple response choices.

The survey will be voluntary. The collection of any personal, identifying information (e.g., first name, last name, address) from respondents will only be used for processing of participants' financial compensation, as allowed by local laws and country regulations, and will be stored in a separate database.

Each individual HCP will be randomly assigned a unique code to access the survey. Each unique code will be deactivated upon first use to prevent the code from being used to complete the survey multiple times. Individuals will not have to actively "decline to complete the survey". Therefore, there will be no ability to track those who decline to participate. Individuals who log into the survey and decline to complete the full survey will be presented with two questions relating to whether non-respondents have prescribed baricitinib and whether they are aware of the important safety information communicated in the HCP Educational Materials and in the DHPC communication. Participants who agree to respond to the survey will begin with a screening module with questions to confirm eligibility.

The survey will be self-administered. For both the internet and paper modalities (where requested), the surveys will be available in the applicable local language.

The survey will include questions in the following categories:

Screening questions:

- *Agreement to participate*
- *Dermatologists or rheumatologists*
- *Current or past employment by Lilly, or any of its affiliates, UBC, IQVIA, the EMA, or any NCA*

Data on demographic characteristics:

- *Geographical location*
- *Years of experience in speciality*
- *Proportion of patients seen with relevant indication for the speciality (ie., proportion of patients seen with either AD or AA for the dermatologists or proportion of patients seen with RA for the rheumatologists)*
- *Prescriber of baricitinib (yes/no)*
- *Number of patients prescribed baricitinib*

Data pertaining to evaluation of the dermatologists and rheumatologists' understanding of the important safety information in the HCP Educational Materials, communication of the important safety information and mitigating actions to patients prescribed baricitinib for the first time, and distribution of the PAC to patients prescribed baricitinib for the first time.

Data pertaining to evaluation of dermatologists' and rheumatologists' understanding of the content of the DHPC.

9.5. Study Size

The target sample size is approximately 200 dermatologists and approximately 200 rheumatologists, leading to a total of approximately 400 completed surveys. This sample size was determined based on providing a precision of ±5% around a response of 50%, based on a two-sided 95% confidence interval (CI) for the full population of 400 surveys. Because precision varies based on the proportion who respond correctly, Table 1 provides a range of expected precision, based on the normal approximation of the binomial CI, for several proportions as well as sample sizes. The greatest variance and, therefore, the least precision, occurs when the observed proportion of responses is 50%, i.e., when p=0.5 in the equation below:

$$p \pm z_{1-\alpha/2}\sqrt{\frac{p(1-p)}{n}}$$

Where p = proportion of interest
α = desired confidence
$z_{1-\alpha/2}$ = 1.96 for 95% confidence
n = sample size

Additional requirements for the same size include:

- Require that at least 50% of respondents from each speciality indicate they have prescribed baricitinib
- The maximum number of completed surveys from any individual country will be set to 80 for each speciality, i.e., maximum of 80 dermatologists from each country and 80 rheumatologists from each country.

Although the sample size is based on the requirements set in the study, the proportion of correct responses cannot be known ahead of time. Since precision depends on both the sample size and the proportion of correct responses, a range of possible precision is presented for different proportions at relevant sample sizes. For analyses by prescriber status, where 200 of each specialty are anticipated, the precision of results will lie within ±7% at worst.

For analysis overall, where 400 surveys will be completed, the precision of results will lie within ±5% at worst. Results by country subgroups cannot be estimated since the total number of completed surveys from each country is not yet known. Further stratification is not planned as the resulting sample sizes would have limited precision. For example, 40 responses resulting from stratifying prescriber status by country would have less precision than ±15.5%.

Table 1. Estimated Precision, by Sample Size and Proportion

Sample size	Proportion of Correct Responses Observed (%)	Precision or Margin of Error* (±%)
40	50	15.5
	70	14.2
	80	12.4
	90	9.3
200	50	6.9
	70	6.4
	80	5.5
	90	4.2
400	50	4.9
	70	4.5
	80	3.9
	90	2.9

* 95% confidence interval, two-sided.

9.6. Data Management

All data collected during the survey will be confidential. UBC's secure web-based proprietary EDC system used for data collection does not include any respondent-identifying information. Respondent identifiers are stored in a separate encrypted electronic database from the survey responses.

The survey is programmed to ensure that respondents cannot go back or skip ahead. The survey will time out after 30 minutes of inactivity. Where possible, statements requiring response and response options are presented in a list and are randomised to minimise positional bias. In addition, the ability to mark only one response is part of the programming for the survey administration and will minimise the occurrence of data entry errors. There will be no follow-up questions to respondents for this project.

Throughout the course of the study, a full back-up of the data will be performed on a nightly basis and cumulative back-ups will also be performed on a weekly basis. Back-up files will be stored at a secure off-site location.

Documentation related, but not limited, to the following will be retained:

- Computer software and hardware development, validation, and maintenance records
- Project specific procedures
- Curriculum vitae and training records of personnel
- Team roster

- Organizational charts
- Audit reports/audit certificates

Note: Standard retention policy for documents is at least 2 years following project closure, unless otherwise required per the contract.

Testing and production data extracted from the EDC database-derived analysis datasets, and generated tables, listings, and figures (TLFs), will be validated, documented, and retained by UBC after the data is exported from the EDC system.

The UBC EDC application provides protection and security. The team incorporates processes, automated and manual tools, and experienced security experts to ensure the protection of all stakeholder and sponsor data. These tools and processes are governed by data privacy and protection standard operating procedures (SOPs) to ensure compliance and adherence. Protection of the data requires that audit trails be under application control for all updates and deletions, and that date and time stamps are available. The UBC EDC maintains an audit trail containing date and time stamps at all times. Security of the application requires data centre and application security which is governed by physical and logical security SOPs. The UBC EDC maintains user and group-level security so that only staff on the Lilly baricitinib team will have access to the system. All web-based applications include secure sockets layer, encryption, and authentication protocols for access. Any remote user to the system must obtain a secure username and password that is only assigned after proper training is completed and authorisation is granted by the appropriate personnel. Remote UBC staff must log in via a secure virtual private network, as well as with a secure username and password. Access is available only to personnel who are provided a username and password, or to survey respondents who are provided a unique study-based code.

Dependability of the application requires that the application have validated and documented evidence that the application does what it is purported to do and will continue to do so. The database will be thoroughly validated and documentation of testing will be completed.

UBC's Information Technology (IT) applications are governed by a development approach to ensure compliance to the United States Food and Drug Administration (FDA) Guidance for Industry-Computerized Systems Used in Clinical Trials in the Title 21 Code of Federal Regulations (CFR) Part 11, Electronic Records; Electronic Signatures, and EudraLex Annex 11: Computerized Systems, and international regulations and standards (e.g., EU Guideline on Good Pharmacovigilance Practices [GVP], International Council for Harmonisation [ICH]) and relevant EMA guidelines. Title 21 CFR Part 11 applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted under any records requirements set forth in Agency regulations. Part 11 also applies to electronic records submitted to the Agency under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act. In accordance with Title 21 CFR Part 11 Department of Health and Human Services Federal Regulations, the EDC application must provide protection, security, and dependability. Protection of the data requires that audit trails be under application control for all updates and deletions, and that date and time stamps are available. Therefore, all associated Title 21 CFR Part 11 requirements are documented including: requirements for data entry, audit trails, date and time stamps, and security. Furthermore, the Title 21 CFR Part 11 checklist, which captures the traceability of the EDC

requirements to the requirements set forth in the Title 21 CFR Part 11, *Electronic Records, Electronic Signatures,* is included in the validation summary report.

No respondent contact information will be included in the tables or in the final report.

9.7. Data Analysis

Data collected from the survey will be reported as descriptive statistics. Frequency distributions with 95% CIs will be calculated for responses to questions that address the knowledge of the KRMs within the HCP Educational Materials (i.e., excluding demographic questions and general questions concerning the HCP Educational Materials and the DHPC).

Survey data will be analysed overall, and stratified by country, speciality, prescriber status (has previously prescribed baricitinib [i.e., prescriber] or has not previously prescribed baricitinib [i.e., potential prescriber]), and by number of patients treated. The cut-off for stratifying results defined by the number of patients prescribed baricitinib, will be based on the distribution of number of prescriptions in the data. This is to ensure that sufficient numbers are available for each stratum. Analysis by experience treating patients with AD/AA or RA will be based on responses to survey Question 4 (number of years practising in speciality : <5, 5–10, 11–15, >15 years) and Questions 5a and 5b (number of patients who have AD/AA or RA : <5, 5–25, >25), described in Annex 1. The cut-off for stratifying results by "high" or "low" experience will be determined on the distribution of prescribers in the cross-categorisation of experience and proportion of patients with the applicable indication.

Responses will be categorised as "Correct response" and "Incorrect response". "I do not know" is categorized as an incorrect response.

For Objective 1, Table 2 outlines these 7 key risk messages, the individual questions within each message, and the criteria for success of each message.

Table 2. Key Risk Messages and Criteria for Success for Objective 1 (HCP Educational Materials).

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
KRM 1: Pregnancy	8a	Correctly responding to the single element of Question 8 for KRM 1.
Question 8*:* Which of the following statements is correct? *Select one only.*		
8a Olumiant (baricitinib) is contraindicated in pregnancy.		
8b Olumiant (baricitinib) is safe to use in pregnancy.		
8c Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment.		
8d I do not know.		
KRM 2: Lipid parameters	9a	

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
Question 9: Which of the following statements is correct? *Please select one option.* **9a** In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected. **9b** There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing. **9c** I do not know.		Correctly responding to the single element of Question 9 for KRM 2.
KRM 3: Infections	10a	Correctly responding to the three elements for Questions 10, 11, and 12 for KRM 3.
Question 10: Which of the following statements is true? *Please select one option.* **10a** Olumiant (baricitinib) increases the potential risk of infection. **10b** Patients can wait to mention any symptoms of infection at their next scheduled clinic visit. **10c** All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics. **10d** I do not know.		
Question 11: Which of the following statements is correct? *Select one only.*	11c	
11a If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued.		
11b Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib).		
11c Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy.		
11d I do not know.		
Question 12: Which of the following statements is correct? *Select one only.*	13a	
12a Caution should be used when treating patients with diabetes with Olumiant (baricitinib).		
12b Olumiant (baricitinib) should never be used in patients over 65 years of age.		
12c I do not know.		
KRM 4: Venous thromboembolism		Correctly responding to the three elements of Question 13 for KRM 4.
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
13a There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib).	False	
13b Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors.	True	
13c Patients should be advised to seek immediately medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism.	True	
KRM 5: Major Adverse Cardiovascular Events		Correctly responding to the three elements of Question 14 for KRM 5.
Question 14: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		
14a There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib).	True	
14b Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors.	False	
14c In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available.	True	
KRM 6: Lymphoma and other Malignancies		Correctly responding to the two elements of Question 15 for KRM 6.
Question 15: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		
15a Lymphoma or other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib).	True	
15b In patients with a past history of malignancy or with other malignancy risk factors, Olumiant (baricitinib) should only be used if no suitable alternative treatments are available.	True	
KRM 7: Dosing		Correctly responding to the three elements of Question 16 for KRM 7
Question 16: For which patients is a 2 mg once daily dose recommended? *Please answer True, False, or I do not know for each of the following statements.*		
16a Patients aged 65 years or over.	True	
16b Patients with depression.	False	
16c Patients at a higher risk of malignancy, venous thromboembolism, and major adverse cardiovascular	True	

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
events or with a history of chronic or recurrent infections.		

Abbreviation: HCP = healthcare professional.

For Objective 2, Table 3 outlines the individual questions for the key risk message and the criteria for success.

Table 3. Key Risk Messages and Criteria for Success for Objective 2 (DHPC)

Key Risk Message (KRM)	Desired Response	Demonstrated Understanding of Message
KRM 8: JAK inhibitor class effect		Correctly responding to the 6 elements of Questions 17, 18 and 19 for KRM 8
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? *Please answer True, False, or I don't know for each of the following statements.*		
17a Major adverse cardiovascular events.	True	
17b Venous thromboembolism.	True	
17c Serious infections.	True	
17d Mortality.	True	
Question 18. Which of the following statements is correct? *Select one only.*	18b	
18a Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression.		
18b Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy.		
18c Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes.		
18d I do not know.		
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*	19a	
19a Periodic skin examination.		
19b Periodic liver ultrasound.		
19c I do not know.		

Abbreviations: DHPC = Direct Healthcare Professional Communication; JAK = Janus kinase.

Among prescribers, the proportion who report the following will be assessed:

- Communication of this information and mitigating actions to patients prescribed baricitinib for the first time, and
- Distribution of the PAC to patients prescribed baricitinib for the first time.

The following information will be reported as part of the analysis using counts and percentages:

- *Survey administration will be performed by country, by speciality and overall:*
    - *The number of survey invitations*
    - *The number of survey invitations/reminders returned due to incorrect mailing/emailing address of dermatologists/rheumatologists invited to participate in the survey*
    - *The number of dermatologists/rheumatologists who responded to the invitation to participate in the survey*
    - *The number of dermatologists/rheumatologists who meet the inclusion criteria for participation in the survey*
    - *The number of dermatologists/rheumatologists who do not meet the inclusion criteria along with the reasons for ineligibility*
    - *The number of dermatologists/rheumatologists who meet the inclusion criteria and completed the survey*
- *Demographic characteristics of participants by country*
    - *Distribution of participants by number of patients currently treated with baricitinib*
- *Responses to questions pertaining to the important safety information (Question 8 to Question 19)*
- *Demonstrated understanding of Key Risk Message 1 to 8.*

For Objective 1, HCPs' understanding of the important safety messages detailed in the HCP Educational Materials, communication of the important safety information and mitigating actions to patients prescribed baricitinib for the first time, and distribution of the PAC to patients prescribed baricitinib for the first time will be analysed by geography, speciality, prescribing status/number of patients treated with baricitinib, and experience with treating patients with the relevant dermatological or rheumatological condition.

A similar analysis will take place for Objective 2.

9.8. Quality Control

Data will be collected using a secure and validated online EDC system designed and built by UBC. A System Development Life Cycle (SDLC) is used for validation that complies with UBC internal IT SOPs. The SDLC is fortified with SOPs addressing validation for all clinical and risk minimisation-related applications. The internet-based repository will be used to store survey data and other relevant programme information. UBC's IT applications are governed by a development approach to ensure compliance with FDA 21 CFR Part 11, international regulations and standards (e.g., EU GVP, ICH) and relevant EMA guidelines. The system is compliant for the entry, storage, handling, analysis and transmission of

electronic information. Respondent-identifying information will be stored separately from the survey responses. At the end of each survey cycle, data will be extracted from the EDC.

Programming will be reviewed by UBC Quality Control and simulated users (User Acceptance Testing) prior to implementation.

At the completion of data collection, data will be extracted from the EDC and mapped to Statistical Analysis Software (SAS) datasets (SAS V9.1.3 or higher). The extracted EDC data will be mapped to SAS datasets ("original" production datasets) as defined in the annotated Data Collection Tools (aDCTs) by a SAS programmer/designee. The mapping of raw data will be validated, as will the programming of the analysis tables created from the raw EDC data. Additionally, the EDC data will also be mapped to SAS datasets by a Server Reporting Services (SSRS) programmer as defined in the aDCTs and validated by the UBC Quality Control Team. These original SAS datasets will be validated by double programming and Quality Control. The validated original SAS datasets will then be used by a SAS programmer to create a set of summary tables and listings according to the SAP text and mock-up tables. If derived analysis datasets are required to produce these summary tables, these will be created and independently validated. All TLF output will be independently validated and documented. Summary tables will be reviewed by the appropriate team members and included in the final report sent to Lilly to be submitted to the PRAC.

UBC has an IT Quality Assurance Group that is responsible for managing and overseeing system/application development and validation, as well as related compliance functions.

9.9. Limitations of the Research Methods

The database of dermatologists and rheumatologists in each country from which the recruitment mailing list is derived is a database of prescribers who have previously agreed to participate in survey research. This approach of only contacting HCPs who have consented to be contacted for research purposes has been taken to be compliant with the General Data Protection Regulation (GDPR). However, there is possible selection bias by not reaching out broadly to all practicing rheumatologists or dermatologists in each of the 3 countries. The difficulties of survey research in the EU because of data protection regulations and possible selection bias issues were highlighted in a White Paper by the International Society for Pharmacoepidemiology and presented at the European Medicine Agency's Workshop on Measuring the Impact of Pharmacovigilance Activities (Madison and Sobel 2016). Participants who have agreed to be included in this type of database may differ in their knowledge and prescribing characteristics from the overall group of practicing clinicians in each country. Given the restrictions of the GDPR that individuals may only be contacted if they have agreed to the contact, it is not possible to contact all HCPs that receive the aRMM materials. Therefore, this type of selection bias is a possibility for all survey-based research where the participants who do respond to the survey may differ from those who do not respond.

The survey recruitment strategies are intended to recruit dermatologists and rheumatologists who report that they are prescribers or potential prescribers of baricitinib. Participants will be self-selected since they will voluntarily respond to the invitation to participate, so the potential exists that those who choose to respond to the survey may differ in their

understanding of the important safety information from those who elect not to participate. This is a common limitation of all studies that rely on voluntary participation. A possible approach to address this potential selection bias will be through the use of a limited non-respondent survey, which will be offered to those who decline to respond to the full survey. Subjects who decline to participate may nonetheless elect to respond to 2 questions aimed at understanding whether they differ in important ways from those who volunteer to respond to the survey. Specifically, these questions will request information on whether non-respondents have prescribed baricitinib and whether they are aware of the important safety information communicated in the HCP Educational Materials and in the DHPC communication.

Among those who volunteer to respond to the survey, recall of information is critical. Inherent in survey research is the reliance on the respondent's recall of whether or not the documents were received. If the respondent says she/he did not receive them, the risk minimisation programme is evaluated as not optimally disseminating the materials. It is possible, however, that respondents may simply not recall receiving these documents even thought they were, in fact, received.

It is also possible that the respondents have acceptable understanding of the important safety information despite not receiving or recalling receipt of the documents. The survey can assess the participants' understanding of the important safety information but cannot clearly determine via which channel they gained the information.

All data from the survey are self-reported and therefore susceptible to possible reporting bias.

9.9.1. Controls to Minimise Bias

A number of controls will be in place to ensure that the survey is conducted and minimise bias, including the following:

- Lists of response options will be randomised to minimise the potential for positional bias.
- The internet surveys will be programmed to ensure that questions are asked in the appropriate sequence, and all questions will be presented in a standard order to reduce exposure bias. Respondents cannot skip ahead or go back to a question once the question has been answered. All questions presented must be answered in order to complete a survey.
- Respondents will be provided with a unique code during the recruitment process in order to gain access to the internet-based systems. The code will be inactivated after use to minimise exposure bias and fraud.

9.10. Other Aspects

Not applicable.

10. Protection of Human Subjects

10.1. Personal Information and Consent

All data collected during the survey will be kept confidential by UBC and used only for the purposes stated in the survey instructions. The collection of any personal, identifying information (first name, last name, address) from respondents will only be used for the processing of the participants' financial compensation. Respondent identifiers are stored in a separate encrypted electronic database from the survey responses. The EDC system used for data collection of the survey responses does not collect any identifiable information. The sponsor will not have access to any personal information collected in relation to this survey.

By answering the first question of the survey ("*Do you agree to participate in this survey?*"), respondents are providing informed consent for participation in the research study.

10.2. Respondent Withdrawal

Respondents can decline to participate or stop taking the survey at any time. Only complete surveys will be included in the analysis.

10.3. Ethics Committee

Approval of this protocol by the respective local Ethics Committee will be sought prior to initiating the survey in each country, where applicable.

10.4. Ethical Conduct of the Study

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor, and follow generally-accepted research practices described in the *Guideline on Good Pharmacovigilance Practices* (*GVP) Module XVI- RMM: Selection of Tools and Effectiveness Indicators* (EMA 2017), *Good Pharmacoepidemiology Practices (GPP)* issued by the International Society for Pharmacoepidemiology (ISPE 2015), *Good Epidemiological Practice* (GEP) guidelines issued by the International Epidemiological Association (Hoffman et al 2019), *International Ethical Guidelines for Epidemiological Research* issued by the Council for International Organisations of Medical Sciences (CIOMS [WWW]), EMA European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) *Guide on Methodological Standards in Pharmacoepidemiology* (ENCePP 2023), and the United States FDA Guidance for Industry: *Good Pharmacovigilance and Pharmacoepidemiologic Assessment* (US FDA 2005).

11. Management and Reporting of Adverse Events/Adverse Reactions

11.1. Primary Data Collection Study

Adverse events will not be actively collected as this study is assessing dermatologists' and rheumatologists' understanding of the important safety information detailed in the HCP Educational Materials, the PAC and the DHPC.

Study personnel and survey respondents are requested to report any suspected adverse reactions (SARs) with any drug to the appropriate party as required in normal practice.

11.2. Product Complaints

Lilly collects product complaints on marketed Lilly products such as drugs, drug/device combinations, medical devices, software as medical device (e.g., mobile medical applications), and comparator product(s) used in post-marketing medical research studies to ensure the safety of study participants, monitor quality, and to facilitate process and product improvements.

For Lilly products under evaluation and/or Lilly products not under evaluation but discovered during the study, study personnel and survey respondents are instructed to report product complaints as they would for products in the marketplace.

For non-Lilly products, such as comparator drugs or medical devices, or concomitant drugs or medical devices, study personnel are instructed to report product complaints as they would for products in the marketplace.

12. Plans for Disseminating and Communicating Study Results

Final reports will be submitted to regulatory agencies. The study, including the final report, will also be registered in the ENCePP Register. The study findings may be submitted to a scientific congress and/or to a peer-reviewed journal.

13. References

[CIOMS] Council for International Organisations of Medical Sciences. *International Ethical Guidelines for Epidemiological Research*. Accessed 08 Sept 2023. https://cioms.ch/publications/product/international-ethical-guidelines-for-epidemiological-studies/

[ENCePP] European Network of Centres for Pharmacoepidemiology and Pharmacovigilance. The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). Guide on methodological standards in pharmacoepidemiology. EMA/95098/2010 Rev. 11. Published July 2023. Accessed 08 Sept 2023. https://www.encepp.eu/standards_and_guidances/documents/01.ENCePPMethodsGuideRev.11.pdf

[EMA] European Medicines Agency. Guideline on good pharmacovigilance practices (GVP) Module XVI – risk minimisation measures: selection of tools and effectiveness indicators. EMA/204715/2012 Rev. 2. Published 28 March 2017. Accessed 08 Sept 2023. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-module-xvi-risk-minimisation-measures-selection-tools_en-3.pdf

Hoffmann W, Lata U, Baumeister SE, Brunger M, Buttmann-Schweiger N, Hardt J, Offmann V, Karch A, Richter A, Schmidt CO, Schmidtmann I, Swart E, van den Berg N. Guidelines and recommendations for ensuring Good Epidemiological Practice (GEP): a guideline developed by the German Society for Epidemiology. *Eur J Epidemiol*. 2019;34(3):301-317.

[ISPE] International Society for Pharmacoepidemiology. Guidelines for good pharmacoepidemiology practices (GPP). Rev. 3. Published June 2015. Accessed 08 Sept 2023. https://www.pharmacoepi.org/resources/policies/guidelines-08027/

Madison T, Sobel R. Evaluating the effectiveness of additional risk minimisation measures via surveys in Europe: challenges and recommendations. Presented at: European Medicines Agency workshop on measuring the impact of pharmacovigilance activities; 06 December 2016, London, UK. https://www.ema.europa.eu/en/documents/presentation/presentation-ispe-paper-evaluating-effectiveness-additional-risk-minimisation-measures-surveys_en.pdf

[US FDA] United States Food and Drug Administration. Guidance for industry: good pharmacovigilance and pharmacoepidemiologic assessment. Published 22 March 2005. Accessed 08 Sept 2023. https://www.fda.gov/files/drugs/published/Good-Pharmacovigilance-Practices-and-Pharmacoepidemiologic-Assessment-March-2005.pdf

Annex 1. List of Standalone Documents

Number	Document Reference Number	Date	Title
1	Appendix I.1		Proposed Surveys (online survey and paper survey)
2	Appendix I.2		Sample Draft Survey Invitation Letter
3	Appendix I.3		Healthcare Professional Educational Materials and the Patient Alert Card
4	Appendix I.4		Direct Healthcare Professional Communication [date]

APPENDIX I.1. SURVEY

SURVEY LEGEND

- * Indicates field is required
- ---------- indicates beginning and end of a unique page.
- **[PAGE TITLE]** indicates new page/ screen (only specify if needed).
- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.
- **(INTERVIEWER)** is used to indicate directions to the phone interviewer and is set in bold, blue text between parentheses. This text appears when content is to be administered by phone only (for example, spontaneous AE reporting).
- **[<MODALITY>]** indicates a section is to be displayed for a specific modality (i.e. Online, Paper).
- **[BEGIN <Section Description>]** and **[END <Section Description>]** represents the beginning and the end of a section (for example, Welcome Page).
- **[BEGIN INCLUSION/EXCLUSION QUESTIONS]** and **[END INCLUSION/EXCLUSION QUESTIONS]** is displayed next to responses that represent the beginning and the end of the inclusion/exclusion survey content.
- **[BEGIN KEY RISK MESSAGE QUESTIONS]** and **[END KEY RISK MESSAGE QUESTIONS]** is displayed next to responses that represent the beginning and the end of the main survey content.
- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless different language is specified with the question.

Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE/RANDOMISE]** is inserted before questions to indicate to the programmer that the responses should be randomized/randomised for the online and survey). Responses such as “I do not know/I do not remember,” “Prefer not to answer,” All of the above” or “None of the above” will always appear at the end of the randomized responses, where applicable.
- **[KEEP IN POSITION]** Indicates that the option / choice will remain in position. Note this is only needed if the list of randomized.
- **[MAKE URL ACTIVE]** Used to indicate that the URL provided should be made into an active link.

- **[EXCLUSIVE]** Used to indicate that the option / choice should unselect all other options / choices in the question.

- 👁 indicates that the free text field will be included in the Free Text Review module.

- **[ANSWER TO Q#]** indicates dynamic text is present. This instruction should be placed on the question where the dynamic text should display. An instruction does not need to be added to the question from which the dynamic text is taken.
- **[TEXT LEN##]** indicates a single line text box with a max length of the number specified. Default is 200 unless otherwise noted.

- **[MULTI LEN##]** indicates a single line text box with a max length of the number specified. Default is 200 unless otherwise noted.

- **[NUM LEN##]** indicates a single line text box with a max length of the number specified, numeric values only.

- **[AMOUNT/TYPE]/[€XX/£XX]** information will be provided by the European Union Project Manager.

- **[DROP-DOWN LIST INPUT WITH COUNTRIES TABLE]** indicates to the programmer that the response should be a drop-down list containing the countries in the table below.

GERMANY	**SWEDEN**	**FRANCE**

[BEGIN SURVEY HELP SECTION]

If you have questions about or problems with the survey, please contact the Help Desk at: olumiantsurveysupport@ubc.com

[END SURVEY HELP SECTION]

[BEGIN WELCOME PAGE]

This survey should take approximately 25 minutes to complete. If you cannot complete the survey at this time, please return when you can. Once you begin the survey you will need to answer all questions; you will not be able to access the survey again if you exit.

Thank you in advance for your participation. Please note the application will time out after 30 minutes of inactivity.

If you are ready to begin the survey at this time, please click continue.

Please note: Do not use the browser's back button during this survey.

[END WELCOME PAGE]

[BEGIN ONLINE PREAMBLE 1]

Disclaimer

Thank you for your interest in this voluntary research survey about Olumiant® (baricitinib) which is being conducted by UBC Late Stage (UK) Limited on behalf of the sponsor, Eli Lilly and Company (Lilly), the marketing authorisation holder of Olumiant. Taking part in this survey is voluntary; you are under no obligation to participate. You may refuse to take the survey or stop taking the survey at any time.
This survey should take approximately 25 minutes to complete. If you cannot complete the survey at this time, please come back when you can. Once you begin the survey, you will need to answer all questions during the same sitting; you will not be able to access the survey again if you exit the survey before answering all survey questions.

How We Use Your Information

This survey is part of a post marketing commitment between Lilly and the European Medicines Agency (EMA) to assess the effectiveness of the materials sent to you to manage the key risks of Olumiant. Your answers to the survey questions will be combined with those from other respondents and reported in anonymous form to Lilly, the EMA, and any other locally applicable regulatory organisations. Your name will not be used in any report. If you are able to complete all inclusion questions as presented, complete all the important safety information questions, and provide your contact information; you will receive financial compensation based on your local rules and regulations. This financial compensation represents the fair market value for your time in connection with completion of the survey. The amount of the financial compensation was not determined by the volume or value of any referrals or business otherwise generated by you. Your name and address will only be used

to send the financial compensation to you once you complete the survey. This survey is voluntary; you are under no obligation to participate.

How We Protect Your Privacy

We respect that the privacy of your personal information is important to you. All the information you provide will be kept strictly confidential. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Your privacy will be protected; however, research survey records may be inspected by the EMA or other regulatory agencies. Your choice to allow Lilly to use your answers to the survey questions is entirely voluntary but necessary to participate.

How to Learn More about the Online Survey

If you have questions about or problems with the survey, please contact the Help Desk at:

olumiantsurveysupport@ubc.com

[END ONLINE PREAMBLE 1]

[BEGIN SCREENING QUESTIONS]

[BEGIN PREAMBLE 2]

Please provide a response to all questions and statements as they are presented.

[END PREAMBLE 2]

1.* Do you agree to take part in this survey about Olumiant® (baricitinib)?

- ○ Yes
- ○ No

[DISPLAY Q1 = No]
[BEGIN PREAMBLE 3]

We understand you are not interested in taking the survey and recognise that your time is valuable; however, we would ask that you consider responding to three brief questions to help assure the scientific generalisability of the survey.

[END PREAMBLE 3]

1a.* Have you ever prescribed Olumiant?

- ○ Yes
- ○ No
- ○ Prefer not to answer

1b.* Are you familiar with the important safety information included in the Olumiant Healthcare Professional Educational Materials?

- ○ Yes

- ○ No
- ○ Prefer not to answer

1c.* Are you familiar with the important safety information included in the recent letter to communicate safety regarding all Janus kinase (JAK) inhibitors of [16 March 2023 France; 17 March 2023 Germany; 21 March 2023 Sweden **[*only date for relevant country will be displayed*]?**

The letter is also known as a Direct Healthcare Professional Communication.

- ○ Yes **[TERMINATE]**
- ○ No **[TERMINATE]**
- ○ Prefer not to answer **[TERMINATE]**

2.* Have you or any of your immediate family members ever worked directly for Eli Lilly and Company (Lilly) or its affiliates, United BioSource, LLC (UBC), IQVIA, the European Medicines Agency (EMA), or any National Competent Authority (NCA)?

- ○ Yes **[TERMINATE]**
- ○ No

3.* What is your practising speciality?

- ○ Dermatologist
- ○ Rheumatologist
- ○ Other. **[TERMINATE]**

[END SCREENING QUESTIONS]

[BEGIN SURVEY CONTENT]

4.* In total, how many years have you been practising in your speciality?

- ○ Less than 5 years
- ○ 5 – 10 years
- ○ 11 – 15 years
- ○ More than 15 years

[DISPLAY Q5a IF Q3 = DERMATOLOGIST]

5a. Approximately, how many patients per month do you see who have either atopic dermatitis or alopecia areata?

- Less than 5
- 5-25
- More than 25

[DISPLAY Q5b IF Q3 = RHEUMATOLOGIST]

5b. Approximately, how many patients per month do you see who have rheumatoid arthritis?

- Less than 5
- 5-25
- More than 25

6* Have you prescribed Olumiant (baricitinib)?

- Yes
- No **[TERMINATE IF X COMPLETE RESPONDENTS HAVE ANSWERED "NO" WHERE X IS A CONFIGURABLE NUMBER – INITIAL QUOTA 100 rheumatologists and 100 dermatologists]**

[DISPLAY IF Q6 = Yes]

7* Approximately, how many patients have you treated in the last six months with Olumiant (baricitinib)?

- None
- 1-5
- 6-10
- More than 10

[BEGIN PREAMBLE 4]

The following questions are about the important safety information associated with the use of Olumiant (baricitinib) as communicated in the Healthcare Professional Educational Materials.

[END PREAMBLE 4]

8. * Which of the following statements is correct?
[RANDOMISE]

8a. ○ Olumiant (baricitinib) is contraindicated in pregnancy

8b. ○ Olumiant (baricitinib) is safe to use in pregnancy

8c. ○ Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment

8d. ○ I do not know **[KEEP IN POSITION]**

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9. * Which of the following statements is correct?
[RANDOMISE]

9a. ○ In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected

9b. ○ There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing

9c. ○ I do not know **[KEEP IN POSITION]**

---

10. * Which of the following statements is true?
[RANDOMISE]

10a. ○ Olumiant (baricitinib) increases the potential risk of infection

10b. ○ Patients can wait to mention any symptoms of infection at their next scheduled clinic visit

10c. ○ All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics

10d. ○ I do not know **[KEEP IN POSITION]**

---

11. * Which of the following statements is correct?
[RANDOMISE]

11a. ○ If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued

11b. ○ Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)

11c. ○ Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy

11d. ○ I do not know **[KEEP IN POSITION]**

12. * Which of the following statements is correct?
[RANDOMISE]

12a. ○ Caution should be used when treating patients with diabetes with Olumiant (baricitinib)

12b. ○ Olumiant (baricitinib) should never be used in patients over 65 of age

12c. ○ I do not know **[KEEP IN POSITION]**

13.* *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*

[RANDOMISE]	**True**	**False**	**I do not know**
13a. * There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)	○	○	○
13b. * Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors	○	○	○
13c. * Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism	○	○	○

---

14. *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*

[RANDOMISE]	**True**	**False**	**I do not know**
14a. * There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)	○	○	○
14b. * Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors	○	○	○
14c. * In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available	○	○	○

---

15. *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*

		True	False	I do not know
15a. *	Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)	○	○	○
15b. *	In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available	○	○	○

---

16. For which patients is a 2mg once daily dose recommended. *Please answer True, False, or I do not know for each statement.*

[RANDOMISE]

		True	False	I do not know
16a. *	Patients aged 65 years or over	○	○	○
16b. *	Patients with depression	○	○	○
16c. *	Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections	○	○	○

---

17. An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.
[RANDOMISE]

		True	False	I do not know
17a. *	Major adverse cardiovascular events	○	○	○
17b. *	Venous thromboembolism	○	○	○
17c. *	Serious infections	○	○	○
17d. *	Mortality	○	○	○

---

18. * Which of the following statements is correct?

[RANDOMISE]

18a. ○ Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression

18b. ○ Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy

18c. ○ Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes

18d. ○ I do not know **[KEEP IN POSITION]**

---

19. * Which of the following is recommended for patients treated with Olumiant (baricitinib)?

[RANDOMISE]

19a. ○ Periodic skin examination

19b. ○ Periodic liver ultrasound

19c. ○ I do not know **[KEEP IN POSITION]**

[BEGIN PREAMBLE 5]

The next set of questions is about the Healthcare Professional Educational Materials for Olumiant (baricitinib). This document contains important information to assist the initial discussion with your patients when prescribing Olumiant.

[BEGIN ONLINE ONLY] To reference the Healthcare Professional Educational Materials click here. [DISPLAY Wave2HcpEducationalMaterial FOR APPROPRIATE LANGUAGE WHEN HYPERLINK IS CLICKED] [END ONLINE ONLY]

[END PREAMBLE 5]

20. * Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?

○ Yes

○ No

[DISPLAY IF Q20 = Yes]

21. * Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?

○ Yes

○ No

- ○ I do not remember

[DISPLAY IF Q21 = Yes]

22. * Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?

- ○ Yes
- ○ No
- ○ I do not remember

BEGIN PREAMBLE 6]

The next set of questions is about the Patient Alert Card. This Patient Alert Card was enclosed with the Healthcare Professional Educational Materials for Olumiant (baricitinib).

[BEGIN ONLINE ONLY] To reference the Patient Alert Card click here. [DISPLAY Wave2PatientAlertCard FOR APPROPRIATE LANGUAGE WHEN HYPERLINK IS CLICKED] [END ONLINE ONLY]

[END PREAMBLE 6]

23. * Prior to today, were you aware of the Patient Alert Card for Olumiant?

- ○ Yes
- ○ No

[DISPLAY IF Q6 = YES AND Q23 = NO]

24. * Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?

- ○ Yes
- ○ No
- ○ I do not know

[DISPLAY IF Q6 = YES AND Q24 = YES]

25. * When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?

- ○ Yes
- ○ No
- ○ I do not know

[BEGIN PREAMBLE 7]

The next set of questions is about the Direct Healthcare Professional Communication regarding all JAK inhibitors. This document contains important information on the class effects of JAK inhibitors.

[BEGIN ONLINE ONLY] To reference the Direct Healthcare Professional Communication click here. [DISPLAY Wave2DHPC FOR APPROPRIATE LANGUAGE WHEN HYPERLINK IS CLICKED] [END ONLINE ONLY]

[END PREAMBLE 7]

26. *Did you receive a copy of the Direct Healthcare Professional communication [France – 16-Mar-2023; Germany – 17-Mar-2023; Sweden – 21-Mar-2023] **[ONLY SHOW DATE FOR RELEVANT COUNTRY]** to communicate safety regarding all JAK inhibitors?

- ○ Yes
- ○ No
- ○ I do not know

[DISPLAY IF Q26 = YES]

27. * Have you read the Direct Healthcare Professional Communication [France – 16-Mar-2023; Germany – 17-Mar-2023; Sweden – 21-Mar-2023] **[ONLY SHOW DATE FOR RELEVANT COUNTRY]** to communicate safety regarding all JAK inhibitors?

- ○ Yes
- ○ No
- ○ I do not know

[END SURVEY CONTENT]

---------- ADVERSE EVENT/PRODUCT COMPLAINT----------

[TELPHONE ONLY: BEGIN AE]

***(INTERVIEWER: PLEASE RECORD IF RESPONDENT SPONTANEOUSLY REPORTED AN ADVERSE EVENT, PRODUCT COMPLAINT, OR MEDICAL INFORMATION REQUEST DURING THE COURSE OF THIS INTERVIEW.)**

- ○ Yes
- ○ No

[END AE]
[DISPLAY REMAINDER OF PAGE IF AE = Yes]

*Enter Safety Event Verbatim **[MULTI LEN 200]** 👁

(INTERVIEWER: Indicate to the respondent that someone may call them back to ask more questions about the adverse event, product complaint, or medical information request that was reported.)

[BEGIN PREAMBLE 8]

We would like to send you [Sweden - 515 SEK; France - 50€; Germany - 50€] [ONLY SHOW CURRENCY FOR RELEVANT COUNTRY] as financial compensation for your time and effort, but need your email address to do so.

[END PREAMBLE 8]

28* Do you agree to provide your contact information for this purpose?

- ○ Yes
- ○ No

[DISPLAY IF Q28 = Yes]
[BEGIN CONTACT INFORMATION]

You are entitled to claim Sweden - 515 SEK; France - 50€; Germany - 50€] [ONLY SHOW CURRENCY FOR RELEVANT COUNTRY] to compensate you for the time taken to complete this survey.
Please enter your email address below to receive financial compensation for participation in this survey about Olumiant (baricitinib).

EMAIL ADDRESS: [TEXT LEN100]

For additional information about UBC's privacy practices, you may visit https://ubc.com/privacy-policy/.

[BEGIN END OF SURVEY MESSAGE]

This completes the survey. Thank you again for your participation.

[END OF SURVEY MESSAGE]
[END SURVEY CONTENT]

PROPOSED PAPER SURVEY

Please provide your **Unique Identification Code (UIC)** included in the original Invitation Letter on each page of the survey: _____

Physician Survey Questionnaire

Please circle or mark one response per question

1. Do you agree to take part in this survey about Olumiant® (baricitinib)?
   - o Yes (Please proceed to question 2)
   - o No (**We understand you are not interested in taking the survey and recognise that your time is valuable; however, we would ask that you consider responding to three brief questions to help assure the scientific generalisability of the survey**. Please proceed to question 1a.)

   1a. Have you ever prescribed Olumiant?
   - o Yes
   - o No
   - o Prefer not to answer

   1b. Are you familiar with the important safety information included in the Olumiant Healthcare Professional Educational Materials?
   - o Yes
   - o No
   - o Prefer not to answer

   1c. Are you familiar with the important safety information included in the letter sent on [16 March 2023 France; 17 March 2023 Germany; 21 March 2023 Sweden] regarding all Janus kinase (JAK) inhibitors. The letter is also known as a Direct Healthcare Professional Communication.
   - o Yes **(You may terminate the survey now)**
   - o No **(You may terminate the survey now)**
   - o Prefer not to answer **(You may terminate the survey now)**

2. Have you or any of your immediate family members ever worked directly for Eli Lilly and

Company (Lilly) or its affiliates, United BioSource, LLC (UBC), IQVIA, the European Medicines Agency (EMA), or any National Competent Authority (NCA)?

- o Yes **(You may terminate the survey now)**
- o No

UIC: _____

3. What is your field of medical practice?
   - o Dermatologist
   - o Rheumatologist
   - o Other **(You may terminate the survey now)**

4. In total, how many years have you been practising in your field?
   - o Less than 5 years
   - o 5 – 10 years
   - o 11 – 15 years
   - o More than 15 years

5. Approximately, how many patients per month do you see who have rheumatoid arthritis?
   - o Less than 5
   - o 5-25
   - o More than 25

6. Have you prescribed Olumiant (baricitinib)?
   - o Yes
   - o No **(You may terminate the survey now)**

7. Approximately, how many patients have you treated in the last six months with Olumiant (baricitinib)?
   - o None
   - o 1-5
   - o 6-10
   - o More than 10

The following questions are about the important safety information associated with the use of Olumiant (baricitinib) as communicated in the Healthcare Professional Educational Materials.

8. Which of the following statements is correct? *Select one only.*
   a. Olumiant (baricitinib) is contraindicated in pregnancy
   b. Olumiant (baricitinib) is safe to use in pregnancy
   c. Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment
   d. I do not know

UIC: _____

9. Which of the following statements is correct? *Please select one option.*
    a. In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected
    b. There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing
    c. I do not know

10. Which of the following statements is true? *Please select one option.*
    a. Olumiant (baricitinib) increases the potential risk of infection
    b. Patients can wait to mention any symptoms of infection at their next scheduled clinic visit
    c. All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics
    d. I do not know

11. Which of the following statements is correct? *Select one only.*
    a. If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued
    b. Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)
    c. Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy
    d. I do not know

12. Which of the following statements is correct? *Select one only.*
    a. Caution should be used when treating patients with diabetes with Olumiant (baricitinib)
    b. Olumiant (baricitinib) should never be used in patients over 65 of age
    c. I do not know

13. *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*

	True	False	I do not know
a. There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)	○	○	○
b. Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors	○	○	○
c. Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism	○	○	○

UIC: _____

14. *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*

	True	False	I do not know
a. There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)	○	○	○
b. Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors	○	○	○
c. In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available	○	○	○

15. *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*

	True	False	I do not know
a. Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)	○	○	○
b. In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available	○	○	○

16. For which patients is a 2mg once daily dose recommended. *Please answer True, False, or I do not know for each statement.*

	True	False	I do not know
a. Patients aged 65 years or over	○	○	○
b. Patients with depression	○	○	○
c. Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections	○	○	○

UIC: _____

17. An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.

	True	False	I do not know
a. Major adverse cardiovascular events	○	○	○
b. Venous thromboembolism	○	○	○
c. Serious infections	○	○	○
d. Mortality	○	○	○

18. Which of the following statements is correct? *Select one only.*

a. Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression
b. Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy
c. Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes
d. I do not know

19. Which of the following recommended for patients treated with Olumiant (baricitinib)?
Select one only.
    a. Periodic skin examination
    b. Periodic liver ultrasound
    c. I do not know

The next set of questions is about the Healthcare Professional Educational Materials for Olumiant (baricitinib). This document contains important information to assist the initial discussion with your patients when prescribing Olumiant. The Healthcare Professional Educational Materials will be mailed upon completion of this survey for reference.

20. Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?
    o Yes
    o No

21. Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?
    o Yes
    o No
    o I do not remember

UIC: _____

22. Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?
    o Yes
    o No
    o I do not remember

The next set of questions is about the Patient Alert Card. This Patient Alert Card was enclosed with the Healthcare Professional Educational Materials for Olumiant (baricitinib). The Patient Alert Card will be mailed upon completion of this survey for reference.

23. Prior to today, were you aware of the Patient Alert Card for Olumiant?
    - o Yes
    - o No

24. Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?
    - o Yes
    - o No
    - o I do not know

25. When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?
    - o Yes
    - o No
    - o I do not know

The next set of questions is about the Direct Healthcare Professional Communication regarding all JAK inhibitors. This document contains important information on the class effects of JAK inhibitors. The Direct Healthcare Professional Communication will be mailed upon completion of this survey for reference.

26. Did you receive a copy of the Direct Healthcare Professional communication [France 16-Mar-2023; Germany 17-Mar-2023; Sweden 21-Mar-2023] to communicate safety regarding all JAK inhibitors?
    - o Yes
    - o No
    - o I do not know

UIC: _____

27. Have you read the Direct Healthcare Professional Communication [France 16-Mar-2023; Germany 17-Mar-2023; Sweden 21-Mar-2023] to communicate safety regarding all JAK inhibitors?
    - o Yes
    - o No
    - o I do not know

That completes the survey. Thank you again for your participation.

APPENDIX I.2. SAMPLE DRAFT INVITATION LETTER

[Date]
[Addressee's name]
[Title]
[Department]
[Hospital Name]
[Street address] [Town]
[City][Post code]
[Country]

Re: Invitation to Participate in Olumiant® (baricitinib) Survey, approved by the European Medicines Agency

Dear Dr. [insert dermatologist/rheumatologist's LAST NAME],

On behalf of Eli Lilly and Company (Lilly), we would like to invite you to participate in a voluntary safety survey about Olumiant (baricitinib), a Janus kinase (JAK)1/JAK2 inhibitor.

The safety survey is part of a Risk Management Plan (RMP) commitment between Lilly and the European Medicines Agency (EMA) to assess the effectiveness of Lilly's communication sent to healthcare professionals to manage the important safety information of Olumiant. The safety survey should take approximately 25 minutes to complete. If you complete the safety survey and provide your contact information, you have the opportunity to receive an electronic gift card worth [**€50/515 SEK** as fair compensation of your time, subject to local rules and regulations.

You may be able to participate if you are currently treating patients with atopic dermatitis, alopecia areata or rheumatoid arthritis. For your convenience, the survey can be completed online at https://www.baricitinibsurvey.com.

You will need the following code when completing the survey: **[UNIQUE CODE]**.

For technical support accessing the survey or if you need a paper version of the survey, please contact the UBC Coordinating Centre at <Insert phone #> between the hours of 9am-5pm local time. You will be asked to provide your survey code.

If participating online, it is possible to take the survey via desktop, laptop, or mobile device using a standard web (i.e. Chrome, Firefox) browser. If using an unsupported browser, an error message will display and it will not be possible to log in.

Why is this important?

In accordance with European regulations, Lilly develops Risk Management Plans (RMPs) for its medications. The RMP for Olumiant outlines the identified and potential risks associated

with use of Olumiant, how these are monitored and what steps are taken to minimise them. In addition to the product labelling, a Healthcare Professional Educational Material, a Patient Alert Card and a Direct Healthcare Professional Communication were developed as additional risk minimisation measures for Olumiant. As part of its regulatory commitment, Lilly is required to assess the effectiveness of these additional risk minimisation measures and report anonymously to the applicable regulatory authorities.

Participation in this safety survey is entirely voluntary. All information that is collected during the course of the safety survey will be kept strictly confidential and in accordance with relevant data protection laws. The results will be reported in aggregate only. Your participation in the safety survey and your answers to the survey questions will not affect your ability to prescribe or currently treat patients to whom Olumiant has been prescribed . You will not be contacted for marketing purposes. Neither Lilly nor its contractors/subcontractors will sell, transfer, or rent your information.

Your assistance with the Olumiant safety survey is greatly appreciated. Thank you for your participation in this important research.

Sincerely,

{Note: Signatory to be determined for each country and customised accordingly}

APPENDIX I.3 Healthcare Professional Educational Materials and the Patient Alert Card

Healthcare Professional Educational Materials - Dermatologists

Information Material for Healthcare Professionals Prescribing Olumiant® (baricitinib)

This document contains important information to assist the initial discussion with your patients when prescribing Olumiant. It should be read in conjunction with the enclosed Summary of Product Characteristics (SmPC).

Olumiant is a selective and reversible janus kinase (JAK)1/2 inhibitor indicated for the treatment of moderate to severe atopic dermatitis (AD) in adult patients who are candidates for systemic therapy and severe alopecia areata (AA) in adult patients.

As part of the initial discussion with your patients, please:
- Provide a **Patient Alert Card** to each patient
- Advise them that the Card should be read in conjunction with the **Patient Information Leaflet**.

The recommended dose of baricitinib is 4 mg once daily.
A dose of 2 mg once daily is recommended for patients:
- at higher risk of venous thromboembolism, major adverse cardiovascular events (MACE), and malignancy,
- aged 65 years and older, and
- with a history of chronic or recurrent infections.

A dose of 4 mg once daily may be considered for patients who do not achieve adequate control of disease activity with 2 mg once daily dose.
A dose of 2 mg once daily should be considered for patients who have achieved sustained control of disease activity with 4 mg once daily and are eligible for dose tapering.

Infections

Olumiant increases the potential risk of infections.

Patients should be instructed to seek immediate medical attention if signs or symptoms suggesting infection appear.

As there is a higher incidence of infections in the elderly and in the diabetic populations in general,

- **caution** should be used when treating the elderly and patients with diabetes.

Changes in Lipid Parameters

Olumiant use is associated with hyperlipidaemia.

Prescribers should monitor the patient's lipid parameters and manage the hyperlipidaemia, if detected.

Venous Thromboembolism

Olumiant increases the risk of venous thrombosis and pulmonary embolism (PE). Olumiant should be used with caution in patients with known risk factors for deep vein thrombosis/PE other than cardiovascular or malignancy risk factors.

Patients should be instructed to seek immediate medical attention if signs or symptoms of deep vein thrombosis/PE appear.

Major Adverse Cardiovascular Events

There is a potentially increased risk of MACE in patients with certain risk factors using JAK inhibitor treatment, including Olumiant.

Thus, Olumiant should only be used if no suitable treatment alternatives are available, in patients:
- 65 years of age and older,
- who are current or past long-term smokers, and
- with other cardiovascular risk factors.

Lymphoma and Other Malignancies

Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant.

Thus, Olumiant should only be used if no suitable treatment alternatives are available, in patients:
- over 65 years of age,
- who are current or past long-term smokers, or

• Olumiant should only be used in patients 65 years of age and older if no suitable treatment alternatives are available. **Advise the patients that** • Olumiant use should be stopped in case of herpes zoster or any other infection that doesn't respond to standard treatment until the event resolves. • they should not be immunised using live attenuated vaccines shortly before or during treatment with Olumiant. Prescribers should screen the patients for viral hepatitis before commencing Olumiant treatment. Active tuberculosis should also be ruled out.	• with other malignancy risk factors (for example, current malignancy or history of malignancy). **Pregnancy and Breast Feeding** Olumiant is contraindicated in pregnancy, as pre-clinical data showed reduced foetal growth and malformations. **Thus,** • physicians should **advise** women of child-bearing potential to use contraception during treatment and for a week after its ending. • Olumiant treatment should be stopped if a planned pregnancy is considered.

Healthcare Professional Educational Materials: Rheumatologists

Information Material for Healthcare Professionals Prescribing Olumiant® (baricitinib)

This document contains important information to assist the initial discussion with your patients when prescribing Olumiant. It should be read in conjunction with the enclosed Summary of Product Characteristics (SmPC).

Olumiant is a selective and reversible janus kinase (JAK)1/2 inhibitor indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti -rheumatic drugs.

As part of the initial discussion with your patients, please:
- Provide a **Patient Alert Card** to each patient
- Advise them that the Card should be read in conjunction with the **Patient Information Leaflet**.

The recommended dose of baricitinib is 4 mg once daily.
A dose of 2 mg once daily is recommended for patients:
- at higher risk of venous thromboembolism, major adverse cardiovascular events (MACE), and malignancy
- aged 65 years and older, and
- with a history of chronic or recurrent infections.

A dose of 4 mg once daily may be considered for patients who do not achieve adequate control of disease activity with 2 mg once daily dose.
A dose of 2 mg once daily should be considered for patients who have achieved sustained control of disease activity with 4 mg once daily and are eligible for dose tapering.

Infections

Olumiant increases the potential risk of infections.

Patients should be instructed to seek immediate medical attention if signs or symptoms suggesting infection appear.

As there is a higher incidence of infections in the elderly and in the diabetic populations in general,

- **caution** should be used when treating the elderly and patients with diabetes.
- Olumiant should only be used in patients 65 years of age and older if no suitable treatment alternatives are available.

Changes in Lipid Parameters

Olumiant use is associated with hyperlipidaemia.

Prescribers should monitor the patient's lipid parameters and manage the hyperlipidaemia, if detected.

Venous Thromboembolism

Olumiant increases the risk of venous thrombosis and pulmonary embolism (PE). Olumiant should be used with caution in patients with known risk factors for deep vein thrombosis/PE other than cardiovascular or malignancy risk factors.

Patients should be instructed to seek immediate medical attention if signs or symptoms of deep vein thrombosis/PE appear.

Major Adverse Cardiovascular Events

There is a potentially increased risk of MACE in patients with certain risk factors using JAK inhibitor treatment, including Olumiant.

Thus, Olumiant should only be used if no suitable treatment alternatives are available, in patients:
- 65 years of age and older,
- who are current or past long-term smokers, and
- with other cardiovascular risk factors.

Lymphoma and Other Malignancies

Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant.

Thus, Olumiant should only be used if no suitable treatment alternatives are available, in patients:
- over 65 years of age,
- who are current or past long-term smokers, or
- with other malignancy risk factors (for example, current malignancy or history of malignancy).

Advise the patient that • Olumiant use should be stopped in case of herpes zoster or any other infection that doesn't respond to standard treatment until the event resolves. • they should not be immunised using live attenuated vaccines shortly before or during treatment with Olumiant. Prescribers should screen the patients for viral hepatitis before commencing Olumiant treatment. Active tuberculosis should also be ruled out.	**Pregnancy and Breast Feeding** Olumiant is contraindicated in pregnancy, as pre-clinical data showed reduced foetal growth and malformations. **Thus,** • physicians should **advise** women of child-bearing potential to use contraception during treatment and for a week after its ending. • Olumiant treatment should be stopped if a planned pregnancy is considered. These points are in line with independent expert European League Against Rheumatism (EULAR) recommendations* *Götestam Skorpen C, Hoeltzenbein M, Tincani A, et al. The EULAR points to consider for use of antirheumatic drugs before pregnancy, and during pregnancy and lactation. *Ann Rheum Dis*. 2016;75(5):795-810. https://doi.org/10.1136/annrheumdis-2015-208840

Patient Alert Card:

Information for Patients about OLUMIANT® (baricitinib) **This document contains important information you should be aware of before and during treatment with Olumiant.** Keep this information with you and share it with other healthcare professionals involved in your medical care or treatment. **Your name:** **Doctor's name** (who prescribed Olumiant)**:** **Doctor's phone number:**	**Pregnancy** • Do not take Olumiant if you are pregnant or suspect you may be pregnant. • Use effective contraception while taking Olumiant (and for 1 week after if you stop treatment). • Tell your doctor immediately if you become (or wish to become) pregnant. **Infections** Olumiant may make an existing infection worse or increase the chance of you getting a new infection or increase the chance of viral reactivation. If you have diabetes or are older than 65, you may have an increased chance of getting infections. The infection can become serious if not treated. Inform your doctor immediately if you get symptoms of infection, such as: • Fever, wounds, feeling more tired than usual, or dental problems. • A cough that won't go away, night sweats, and weight loss. These could be symptoms of tuberculosis (an infectious disease of the lungs). • A painful skin rash with blisters. This could be a sign of a herpes zoster infection. **Non-melanoma skin cancer** Non-melanoma skin cancer has been observed in patients taking Olumiant. If new skin lesions appear during or after therapy or if existing lesions change appearance, tell your doctor. **Blood clots** Olumiant may cause a condition in which a blood clot forms in your leg that may travel to your lungs. Inform your doctor

	immediately if you experience any of the following symptoms: • Swelling or pain in one leg or arm • Warmth or redness in one leg or arm • Shortness of breath which is unexpected • Rapid breathing • Chest pain **Heart attack or stroke** Inform your doctor immediately if you experience any of the following: • Severe chest pain or tightness (that may spread to arms, jaw, neck, back) • Shortness of breath • Cold sweat • One-sided weakness in arm and/or leg • Slurred speech

APPENDIX I.4 Direct Healthcare Professional Communication

<date>

Cibinqo (abrocitinib), Jyseleca (filgotinib), Olumiant (baricitinib), Rinvoq (upadacitinib) and Xeljanz (tofacitinib) – Updated recommendations to minimise the risks of malignancy, major adverse cardiovascular events, serious infections, venous thromboembolism and mortality with use of Janus kinase inhibitors (JAKi).

Dear Healthcare Professional,

AbbVie, Galapagos, Lilly and Pfizer in agreement with the European Medicines Agency and the <National Competent Authority> would like to inform you of the following:

Summary

- An increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality has been observed in patients with rheumatoid arthritis (RA) with certain risk factors using JAKi treatment com**pared to TNFα inhibitors.**
- These risks are considered class effects and relevant across all approved indications of JAKi in inflammatory and dermatologic diseases.
- These JAKi should only be used if no suitable treatment alternatives are available in patients:
    - 65 years of age and older;
    - who are current or past long-time smokers;
    - with other cardiovascular or malignancy risk factors.
- JAKi should be used with caution in patients with VTE risk factors other than those listed above.
- Dosing recommendations are revised for some patient groups with risk factors.
- Periodic skin examination is recommended for all patients.
- Prescribers should discuss with patients the risks associated with the use of JAKi.

Background on the safety concern

The JAKi Cibinqo (abrocitinib), Jyseleca (filgotinib), Olumiant (baricitinib), Rinvoq (upadacitinib) and Xeljanz (tofacitinib) are approved for the treatment of several chronic inflammatory disorders (rheumatoid arthritis (RA), psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, ulcerative colitis, atopic dermatitis, and alopecia areata). The approved use differs for the different products, as outlined in the respective product information.

In March 2021, a Direct Healthcare Professional Communication (DHPC) for Xeljanz (tofacitinib)[1] was sent to healthcare professionals, informing them that data from a completed clinical trial (A3921133)[2] in patients with RA who were 50 years of age or older with at least one additional cardiovascular risk factor, suggest a higher risk of major adverse cardiovascular events (MACE) and malignancies (excluding non-melanoma skin cancer (NMSC)) with tofacitinib as compared to patients treated with a TNF-alpha inhibitor.

An additional DHPC[3] was sent in July 2021 to inform about an increased incidence of myocardial infarction, lung cancer, and lymphoma with tofacitinib compared to TNF-alpha inhibitors observed in the same clinical trial, as well as adopted recommendations for the product information of tofacitinib.

Preliminary findings from an observational study (B023) involving another JAK inhibitor, Olumiant (baricitinib), also suggest an increased risk of major cardiovascular events and VTE in patients with RA treated with Olumiant compared with those treated with TNF-alpha inhibitors.

Following the finalization of the review procedure of the available data across these five JAKi by EMA, recommendations have been adopted as specified in the "summary" above. The product information and the educational materials for healthcare professional and patients is being updated accordingly.

This letter is not intended as a complete description of the benefits and risks related to the use of these products. For further details, please refer to the updated SmPC for the respective products.

Call for reporting

< to be filled nationally>

Healthcare providers and patients are encouraged to report adverse reactions in accordance with the national spontaneous reporting system. <to be filled nationally> Please find the relevant contact for each product in the table below.

Product	Cibinqo (abrocitinib)	Jyseleca (filgotinib)	Olumiant (baricitinib)	Rinvoq (upadacitinib)	Xeljanz (tofacitinib)
MAH	Pfizer	Galapagos	Lilly	AbbVie	Pfizer
Telephone number					
Email address					

Company contact point

< to be filled nationally>

[1] https://www.ema.europa.eu/en/medicines/dhpc/xeljanz-tofacitinib-initial-clinical-trial-results-increased-risk-major-adverse-cardiovascular
[2] Ytterberg, Steven R., et al. "Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis." *New England Journal of Medicine* 386.4 (2022): 316-326.
[3] https://www.ema.europa.eu/en/medicines/dhpc/xeljanz-tofacitinib-increased-risk-major-adverse-cardiovascular-events-malignancies-use-tofacitinib

Product	Cibinqo (abrocitinib)	Jyseleca (filgotinib)	Olumiant (baricitinib)	Rinvoq (upadacitinib)	Xeljanz (tofacitinib)
MAH	Pfizer	Galapagos	Lilly	AbbVie	Pfizer
Website address					
Postal address					

Annex 2. ENCePP Checklist for Study Protocols

Study title: Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant® (baricitinib) a JAK1/2 inhibitor

EU PAS Register® number: EUPAS43239
Study reference number (if applicable): I4V-MC-B025

Section 1: Milestones	Yes	No	N/A	Section Number
1.1 Does the protocol specify timelines for				
1.1.1 Start of data collection[4]	☒	☐	☐	9
1.1.2 End of data collection[5]	☒	☐	☐	9
1.1.3 Progress report(s)	☐	☐	☒	
1.1.4 Interim report(s)	☐	☐	☒	
1.1.5 Registration in the EU PAS Register®	☒	☐	☐	9
1.1.6 Final report of study results.	☒	☐	☐	9

Comments:

Section 2: Research question	Yes	No	N/A	Section Number
2.1 Does the formulation of the research question and objectives clearly explain:	☒	☐	☐	8
2.1.1 Why the study is conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	7
2.1.2 The objective(s) of the study?	☒	☐	☐	8
2.1.3 The target population? (i.e. population or subgroup to whom the study results are intended to be generalised)	☒	☐	☐	9.3
2.1.4 Which hypothesis(-es) is (are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

The study will be descriptive and there will not be hypothesis testing

[4] Date from which information on the first study is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[5] Date from which the analytical dataset is completely available.

Section 3: Study design		Yes	No	N/A	Section Number
3.1	Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	9.1
3.2	Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	9.1
3.3	Does the protocol specify measures of occurrence? (e.g., rate, risk, prevalence)	☒	☐	☐	9.7
3.4	Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☐	☐	☒	
3.5	Does the protocol describe the approach for the collection and reporting of adverse events/adverse reactions? (e.g. adverse events that will not be collected in case of primary data collection)	☒	☐	☐	11

Comments:

Healthcare Professionals' answers will be categorised as "correct" or "incorrect". The frequency of "correct" answers will be calculated for each question that addresses the study objective.

Section 4: Source and study populations		Yes	No	N/A	Section Number
4.1	Is the source population described?	☒	☐	☐	9.2
4.2	Is the planned study population defined in terms of:				
	4.2.1 Study time period	☒	☐	☐	6 & 9.2
	4.2.2 Age and sex	☐	☒	☐	9.4
	4.2.3 Country of origin	☒	☐	☐	9.4
	4.2.4 Disease/indication	☒	☐	☐	9.4
	4.2.5 Duration of follow-up	☐	☐	☒	
4.3	Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	9.2.1 & 9.4

Comments:

4.2.2 – HCP participant age will not be collected per PRAC feedback.

Section 5: Exposure definition and measurement		Yes	No	N/A	Section Number
5.1	Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☐	☐	☒	
5.2	Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☐	☐	☒	

Section 5: Exposure definition and measurement	Yes	No	N/A	Section Number
5.3 Is exposure categorised according to time windows?	☐	☐	☒	
5.4 Is intensity of exposure addressed? (e.g. dose, duration)	☐	☐	☒	
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.6 Is (are) (an) appropriate comparator(s) identified?	☐	☐	☒	

Comments:

Section 6: Outcome definition and measurement	Yes	No	N/A	Section Number
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	8
6.2 Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	9.7
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☒	☐	☐	9.5
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYS, health care services utilisation, burden of disease or treatment, compliance, disease management)	☐	☐	☒	

Comments:

Section 7: Bias	Yes	No	N/A	Section Number
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☐	☐	☒	
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☒	☐	☐	9.4 & 9.9
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☒	☐	☐	9.9.1

Comments:

Section 8: Effect measure modification	Yes	No	N/A	Section Number
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☐	☐	☒	

Comments:

Section 9: Data sources	Yes	No	N/A	Section Number
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☐	☐	☒	
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview including scales and questionnaires, vital statistics)	☐	☐	☒	
9.1.3 Covariates and other characteristics?	☐	☐	☒	
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☐	☐	☒	
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☐	☐	☒	
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☐	☐	☒	
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☐	☐	☒	
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☐	☐	☒	
9.3.3 Covariates and other characteristics?	☐	☐	☒	
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☐	☐	☒	

Comments:

Section 10: Analysis plan	Yes	No	N/A	Section Number
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	9.7
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	9.5

Section 10: Analysis plan	Yes	No	N/A	Section Number
10.3 Are descriptive analyses included?	☒	☐	☐	9.7
10.4 Are stratified analyses included?	☒	☐	☐	9.7
10.5 Does the plan describe methods for analytic control of confounding?	☐	☐	☒	
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☐	☐	☒	
10.7 Does the plan describe methods for handling missing data?	☐	☐	☒	
10.8 Are relevant sensitivity analyses described?	☐	☐	☒	

Comments:

Only completed, surveys will be included in the analysis, therefore there would not be missing data

Section 11: Data management and quality control	Yes	No	N/A	Section Number
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	9.8
11.2 Are methods of quality assurance described?	☒	☐	☐	9.8
11.3 Is there a system in place for independent review of study results?	☐	☐	☒	

Comments:

Section 12: Limitations	Yes	No	N/A	Section Number
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☒	☐	☐	9.9
12.1.2 Information bias?	☒	☐	☐	9.9
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods).	☐	☐	☒	
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	9.2 & 9.4

Comments:

Section 13: Ethical/data protection issues	Yes	No	N/A	Section Number
13.1 Have requirements of Ethics Committee/ Institutional Review Board been described?	☒	☐	☐	10
13.2 Has any outcome of an ethical review procedure been addressed?	☐	☐	☒	
13.3 Have data protection requirements been described?	☒	☐	☐	10.1

Comments:

Section 14: Amendments and deviations	Yes	No	N/A	Section Number
14.1 Does the protocol include a section to document amendments and deviations?	☒	☐	☐	5

Comments:

Section 15: Plans for communication of study results	Yes	No	N/A	Section Number
15.1 Are plans described for communicating study results (e.g. to regulatory authorities)?	☒	☐	☐	12
15.2 Are plans described for disseminating study results externally, including publication?	☒	☐	☐	12

Comments:

Name of the main author of the protocol: _____

Date: dd/Month/year

Signature: _____

Approved on 01 Mar 2024 GMT

Annex 3. Additional Information

Not applicable.

Approved on 01 Mar 2024 GMT

Annex 2. Additional Information

Appendix 1.2: Final Tables and Listings

Table 1.1: Survey Administration Statistics

Parameter, n (%)	Sweden	France	Germany	Spain	Overall
Rheumatologists					
Number of Survey invitations[a]	1,100	4,811	4,242	1,705	11,858
All Respondents[b]	35 (3.2)	88 (1.8)	95 (2.2)	72 (4.2)	290 (2.4)
Eligible Respondents[d]	31 (88.6)	83 (94.3)	88 (92.6)	66 (91.7)	268 (92.4)
Completed the survey[d]	28 (80.0)	81 (92.0)	80 (84.2)	59 (81.9)	248 (85.5)
Did not complete the survey[d]	3 (8.6)	2 (2.3)	8 (8.4)	7 (9.7)	20 (6.9)
Respondents not eligible[c, d]	4 (11.4)	5 (5.7)	7 (7.4)	6 (8.3)	22 (7.6)
Dermatologists					
Number of Survey invitations[a]	1,700	10,296	8,386	3,209	23,591
All Respondents[b]	52 (3.1)	83 (0.8)	151 (1.8)	102 (3.2)	388 (1.6)
Eligible Respondents[d]	49 (94.2)	72 (86.7)	140 (92.7)	89 (87.3)	350 (90.2)
Completed the survey[d]	46 (88.5)	72 (86.7)	131[e] (86.8)	84 (82.4)	333 (85.8)
Did not complete the survey[d]	3 (5.8)	0	9 (6.0)	5 (4.9)	17 (4.4)
Respondents not eligible[c, d]	3 (5.8)	11 (13.3)	11 (7.3)	13 (12.7)	38 (9.8)
Number of Survey invitations returned (includes both Rheumatologist and Dermatologist)	11	384	43	0	438

Source: Appendix X, Table 1.1
[a] Number of total survey invitations sent, including reminder invitations sent when an HCP had not yet responded.
[b] Number of respondents who accessed the survey. Percentage is based on the number of invitations provided to HCPs.
[c] Number of respondents who did not meet eligibility criteria or did not complete eligibility questions. The responses to the eligibility criteria with the reason for ineligibility are presented in Table 1.2.
[d] Percentages are based on the number of all respondents.
[e] While 131 dermatologists from Germany completed the survey, only the first 80 were included in primary analysis to match protocol specifications. A sensitivity analysis of the Key Risk Message understanding by country includes all 131 respondents.

Table 1.2: Survey Participant Eligibility Results - All Respondents

Question	Sweden (N=87) n (%)	France (N=171) n (%)	Germany (N=246) n (%)	Spain (N=174) n (%)	Overall (N=678) n (%)
Question 1: Do you agree to take part in this survey about Olumiant® (baricitinib)?					
Yes	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
No	0	0	0	0	0
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 1a: Have you ever prescribed Olumiant?					
Yes	0	0	0	0	0
No	0	0	0	0	0
Prefer not to answer	0	0	0	0	0
N/A (answered 'Yes' to Question 1)	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 1b: Are you familiar with the important safety information included in the Olumiant Healthcare Professional Educational Materials?					
Yes	0	0	0	0	0
No	0	0	0	0	0
Prefer not to answer	0	0	0	0	0
N/A (answered 'Yes' to Question 1)	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 1c: Are you familiar with the important safety information included in the recent letter to communicate safety regarding all Janus kinase (JAK) inhibitors of [16 March 2023 France; 17 March 2023 Germany; 21 March 2023 Sweden]					
Yes	0	0	0	0	0
No	0	0	0	0	0
Prefer not to answer	0	0	0	0	0
N/A (answered 'Yes' to Question 1)	84 (96.6)	160 (93.6)	232 (94.3)	165 (94.8)	641 (94.5)
Discontinued	3 (3.4)	11 (6.4)	14 (5.7)	9 (5.2)	37 (5.5)
Question 2: Have you or any of your immediate family members ever worked directly for Eli Lilly and Company (Lilly) or its affiliates, United Biosource, LLC (UBC), IQVIA, the European Medicines Agency (EMA), or any National Competent Authority (NCA)?					
Yes[a]	2 (2.3)	3 (1.8)	2 (0.8)	8 (4.6)	15 (2.2)
No	81 (93.1)	157 (91.8)	230 (93.5)	156 (89.7)	624 (92.0)
Discontinued	4 (4.6)	11 (6.4)	14 (5.7)	10 (5.7)	39 (5.8)
Question 3: What is your practising speciality?					

Table 1.2: Survey Participant Eligibility Results - All Respondents

Question	Sweden (N=87) n (%)	France (N=171) n (%)	Germany (N=246) n (%)	Spain (N=174) n (%)	Overall (N=678) n (%)
Dermatologist	49 (56.3)	74 (43.3)	140 (56.9)	89 (51.1)	352 (51.9)
Rheumatologist	31 (35.6)	83 (48.5)	88 (35.8)	66 (37.9)	268 (39.5)
Other[a]	1 (1.1)	0	2 (0.8)	1 (0.6)	4 (0.6)
Question not asked[b]	2 (2.3)	3 (1.8)	2 (0.8)	8 (4.6)	15 (2.2)
Discontinued	4 (4.6)	11 (6.4)	14 (5.7)	10 (5.7)	39 (5.8)
Question 6: Have you prescribed Olumiant (baricitinib)?					
Yes	55 (63.2)	127 (74.3)	197 (80.1)	139 (79.9)	518 (76.4)
No	25 (28.7)	28 (16.4)	31 (12.6)	16 (9.2)	100 (14.7)
Question not asked[b]	3 (3.4)	3 (1.8)	4 (1.6)	9 (5.2)	19 (2.8)
Discontinued	4 (4.6)	13 (7.6)	14 (5.7)	10 (5.7)	41 (6.0)

Source: Appendix X, Table 1.2
Note: This table include all dermatologists from Germany who completed the survey.
Note: Respondents are designated "discontinued" if they did not answer all eligibility questions and were not identified as ineligible based on responses to previous questions. Once respondents were designated as "discontinued", they were counted as such in all subsequent eligibility questions.
Note: Question 1a, 1b and 1c have been answered by only those not agreeing to participate in survey.
[a] These responses were not consistent with survey eligibility and thus indicated the HCP was ineligible to participate in the survey.
[b] Question not asked due to the skip pattern in the survey or previous question termination.

Table 2: Description of Eligible Respondents - Completed Surveys

Question	Sweden (N=74) n (%)	France (N=153) n (%)	Germany (N=160) n (%)	Spain (N=143) n (%)	Overall (N=530) n (%)
Question 4: In total, how many years have you been practising in your speciality?					
Less than 5 years	18 (24.3)	38 (24.8)	40 (25.0)	40 (28.0)	136 (25.7)
5 – 10 years	26 (35.1)	45 (29.4)	43 (26.9)	42 (29.4)	156 (29.4)
11 – 15 years	11 (14.9)	24 (15.7)	31 (19.4)	29 (20.3)	95 (17.9)
More than 15 years	19 (25.7)	46 (30.1)	46 (28.8)	32 (22.4)	143 (27.0)
Question 5a: Approximately, how many patients per month do you see who have either atopic dermatitis or alopecia areata?[a]					
Less than 5	1 (2.2)	5 (6.9)	3 (3.8)	2 (2.4)	11 (3.9)
5-25	34 (73.9)	46 (63.9)	34 (42.5)	32 (38.1)	146 (51.8)
>25	11 (23.9)	21 (29.2)	43 (53.8)	50 (59.5)	125 (44.3)
N/A (answered 'Rheumatologist' to Question 3)	28	81	80	59	248
Question 5b: Approximately, how many patients per month do you see who have rheumatoid arthritis?[a]					
0-5	0	6 (7.4)	0	1 (1.7)	7 (2.8)
5-25	5 (17.9)	41 (50.6)	4 (5.0)	15 (25.4)	65 (26.2)
>25	23 (82.1)	34 (42.0)	76 (95.0)	43 (72.9)	176 (71.0)
N/A (answered 'Dermatologist' to Question 3)	46	72	80	84	282
Question 6: Have you prescribed Olumiant (baricitinib)?					
Yes	51 (68.9)	125 (81.7)	138 (86.3)	128 (89.5)	442 (83.4)
No	23 (31.1)	28 (18.3)	22 (13.8)	15 (10.5)	88 (16.6)
Question 7: Approximately, how many patients have you treated in the last six months with Olumiant (baricitinib)?					
None	1 (2.0)	10 (8.0)	1 (0.7)	2 (1.6)	14 (3.2)
1-5	38 (74.5)	75 (60.0)	57 (41.3)	53 (41.4)	223 (50.5)
6-10	8 (15.7)	24 (19.2)	29 (21.0)	36 (28.1)	97 (21.9)
More than 10	4 (7.8)	16 (12.8)	51 (37.0)	37 (28.9)	108 (24.4)

Table 2: Description of Eligible Respondents - Completed Surveys

Question	Sweden (N=74) n (%)	France (N=153) n (%)	Germany (N=160) n (%)	Spain (N=143) n (%)	Overall (N=530) n (%)
N/A (answered 'No' to Question 6)	23	28	22	15	88

Source: Appendix X, Table 2
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 3: Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
Question 8: Which of the following statements is correct? *Select one only.*	
Olumiant (baricitinib) is contraindicated in pregnancy[a]	387 (73.0) [69.0-76.8]
Olumiant (baricitinib) is safe to use in pregnancy	7 (1.3)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	105 (19.8)
I do not know.	31 (5.8)
Question 9: Which of the following statements is correct? *Please select one option.*	
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	479 (90.4) [87.5-92.8]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	31 (5.8)
I do not know	20 (3.8)
Question 10: Which of the following statements is true? *Please select one option.*	
Olumiant (baricitinib) increases the potential risk of infection[a]	507 (95.7) [93.6-97.2]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	11 (2.1)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0
I do not know	12 (2.3)
Question 11: Which of the following statements is correct? *Select one only.*	
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	2 (0.4)
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	16 (3.0)
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	502 (94.7) [92.5-96.5]
I do not know	10 (1.9)
Question 12: Which of the following statements is correct? *Select one only.*	
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	415 (78.3) [74.5-81.7]

Table 3: Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
Olumiant (baricitinib) should never be used in patients over 65 of age	65 (12.3)
I do not know	50 (9.4)
Question 13: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***	
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)	
True	59 (11.1)
False[a]	444 (83.8) [80.4-86.8]
I don't know	27 (5.1)
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors	
True[a]	515 (97.2) [95.4-98.4]
False	10 (1.9)
I don't know	5 (0.9)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism	
True[a]	528 (99.6) [98.6-100.0]
False	0
I don't know	2 (0.4)
Question 14: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***	
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)	
True[a]	485 (91.5) [88.8-93.7]
False	31 (5.8)
I don't know	14 (2.6)
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors	
True	154 (29.1)
False[a]	354 (66.8) [62.6-70.8]

Table 3: Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
I don't know	22 (4.2)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available	
True[a]	409 (77.2) [73.4-80.7]
False	89 (16.8)
I don't know	32 (6.0)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***	
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)	
True[a]	380 (71.7) [67.7-75.5]
False	76 (14.3)
I don't know	74 (14.0)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available	
True[a]	468 (88.3) [85.3-90.9]
False	34 (6.4)
I don't know	28 (5.3)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***	
16a: Patients aged 65 years or over	
True[a]	421 (79.4) [75.7-82.8]
False	65 (12.3)
I don't know	44 (8.3)
16b: Patients with depression	
True	44 (8.3)
False[a]	392 (74.0) [70.0-77.7]
I don't know	94 (17.7)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections	

Table 3: Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
True[a]	389 (73.4) [69.4-77.1]
False	86 (16.2)
I don't know	55 (10.4)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.	
17a: Major adverse cardiovascular events	
True[a]	427 (80.6) [76.9-83.9]
False	65 (12.3)
I don't know	38 (7.2)
17b: Venous thromboembolism	
True[a]	488 (92.1) [89.4-94.2]
False	25 (4.7)
I don't know	17 (3.2)
17c: Serious infections	
True[a]	155 (29.2) [25.4-33.3]
False	300 (56.6)
I don't know	75 (14.2)
17d: Mortality	
True[a]	98 (18.5) [15.3-22.1]
False	315 (59.4)
I don't know	117 (22.1)
Question 18: Which of the following statements is correct? *Select one only.*	
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	31 (5.8)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	321 (60.6) [56.3-64.8]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	38 (7.2)
I do not know	140 (26.4)

Table 3: Responses to all Questions Related to the Understanding of the Important Safety Information - Completed Surveys

Question	Respondents (N=530) n (%) [95% CI]
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*	
Periodic skin examination[a]	415 (78.3) [74.5-81.7]
Periodic liver ultrasound	44 (8.3)
I do not know	71 (13.4)

Source: Appendix X, Table 3
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] Correct response.

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
Question 8: Which of the following statements is correct? *Select one only.*					
Olumiant (baricitinib) is contraindicated in pregnancy[a]	51 (68.9) [57.1-79.2]	123 (80.4) [73.2-86.4]	161 (76.3) [70.0-81.9]	94 (65.7) [57.3-73.5]	429 (73.8) [70.1-77.4]
Olumiant (baricitinib) is safe to use in pregnancy	0	1 (0.7)	2 (0.9)	4 (2.8)	7 (1.2)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	16 (21.6)	20 (13.1)	37 (17.5)	38 (26.6)	111 (19.1)
I do not know.	7 (9.5)	9 (5.9)	11 (5.2)	7 (4.9)	34 (5.9)
Question 9: Which of the following statements is correct? *Please select one option.*					
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	62 (83.8) [73.4-91.3]	138 (90.2) [84.3-94.4]	188 (89.1) [84.1-93.0]	133 (93.0) [87.5-96.6]	521 (89.7) [86.9-92.0]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	6 (8.1)	10 (6.5)	14 (6.6)	7 (4.9)	37 (6.4)
I do not know	6 (8.1)	5 (3.3)	9 (4.3)	3 (2.1)	23 (4.0)

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
Question 10: Which of the following statements is true? *Please select one option.*					
Olumiant (baricitinib) increases the potential risk of infection[a]	70 (94.6) [86.7-98.5]	147 (96.1) [91.7-98.5]	203 (96.2) [92.7-98.3]	134 (93.7) [88.4-97.1]	554 (95.4) [93.3-96.9]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	1 (1.4)	2 (1.3)	4 (1.9)	7 (4.9)	14 (2.4)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0	0	0	0	0
I do not know	3 (4.1)	4 (2.6)	4 (1.9)	2 (1.4)	13 (2.2)
Question 11: Which of the following statements is correct? *Select one only.*					
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	0	1 (0.7)	2 (0.9)	0	3 (0.5)
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	3 (4.1)	2 (1.3)	3 (1.4)	9 (6.3)	17 (2.9)

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	67 (90.5) [81.5-96.1]	148 (96.7) [92.5-98.9]	204 (96.7) [93.3-98.7]	132 (92.3) [86.7-96.1]	551 (94.8) [92.7-96.5]
I do not know	4 (5.4)	2 (1.3)	2 (0.9)	2 (1.4)	10 (1.7)
Question 12: Which of the following statements is correct? *Select one only.*					
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	52 (70.3) [58.5-80.3]	113 (73.9) [66.1-80.6]	165 (78.2) [72.0-83.6]	125 (87.4) [80.8-92.4]	455 (78.3) [74.7-81.6]
Olumiant (baricitinib) should never be used in patients over 65 of age	11 (14.9)	28 (18.3)	22 (10.4)	9 (6.3)	70 (12.0)
I do not know	11 (14.9)	12 (7.8)	24 (11.4)	9 (6.3)	56 (9.6)
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*					
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)					
True	7 (9.5)	14 (9.2)	30 (14.2)	17 (11.9)	68 (11.7)
False[a]	63 (85.1) [75.0-92.3]	132 (86.3) [79.8-91.3]	169 (80.1) [74.1-85.3]	120 (83.9) [76.9-89.5]	484 (83.3) [80.0-86.2]
I don't know	4 (5.4)	7 (4.6)	12 (5.7)	6 (4.2)	29 (5.0)

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors					
True[a]	68 (91.9) [83.2-97.0]	149 (97.4) [93.4-99.3]	206 (97.6) [94.6-99.2]	140 (97.9) [94.0-99.6]	563 (96.9) [95.1-98.2]
False	2 (2.7)	3 (2.0)	4 (1.9)	3 (2.1)	12 (2.1)
I don't know	4 (5.4)	1 (0.7)	1 (0.5)	0	6 (1.0)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism					
True[a]	73 (98.6) [92.7-100.0]	152 (99.3) [96.4-100.0]	211 (100.0) [98.3-100.0]	143 (100.0) [97.5-100.0]	579 (99.7) [98.8-100.0]
False	0	0	0	0	0
I don't know	1 (1.4)	1 (0.7)	0	0	2 (0.3)
Question 14: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***					
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)					
True[a]	64 (86.5) [76.5-93.3]	137 (89.5) [83.6-93.9]	195 (92.4) [88.0-95.6]	135 (94.4) [89.3-97.6]	531 (91.4) [88.8-93.5]
False	7 (9.5)	9 (5.9)	8 (3.8)	8 (5.6)	32 (5.5)
I don't know	3 (4.1)	7 (4.6)	8 (3.8)	0	18 (3.1)

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors					
True	21 (28.4)	52 (34.0)	64 (30.3)	35 (24.5)	172 (29.6)
False[a]	50 (67.6) [55.7-78.0]	94 (61.4) [53.2-69.2]	136 (64.5) [57.6-70.9]	104 (72.7) [64.7-79.8]	384 (66.1) [62.1-69.9]
I don't know	3 (4.1)	7 (4.6)	11 (5.2)	4 (2.8)	25 (4.3)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available					
True[a]	47 (63.5) [51.5-74.4]	136 (88.9) [82.8-93.4]	168 (79.6) [73.5-84.8]	94 (65.7) [57.3-73.5]	445 (76.6) [72.9-80.0]
False	18 (24.3)	9 (5.9)	30 (14.2)	44 (30.8)	101 (17.4)
I don't know	9 (12.2)	8 (5.2)	13 (6.2)	5 (3.5)	35 (6.0)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***					
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)					
True[a]	54 (73.0) [61.4-82.6]	104 (68.0) [60.0-75.3]	153 (72.5) [66.0-78.4]	105 (73.4) [65.4-80.5]	416 (71.6) [67.7-75.2]
False	9 (12.2)	29 (19.0)	30 (14.2)	16 (11.2)	84 (14.5)
I don't know	11 (14.9)	20 (13.1)	28 (13.3)	22 (15.4)	81 (13.9)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available					

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
True[a]	63 (85.1) [75.0-92.3]	138 (90.2) [84.3-94.4]	184 (87.2) [81.9-91.4]	125 (87.4) [80.8-92.4]	510 (87.8) [84.8-90.3]
False	5 (6.8)	7 (4.6)	17 (8.1)	14 (9.8)	43 (7.4)
I don't know	6 (8.1)	8 (5.2)	10 (4.7)	4 (2.8)	28 (4.8)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***					
16a: Patients aged 65 years or over					
True[a]	58 (78.4) [67.3-87.1]	122 (79.7) [72.5-85.8]	155 (73.5) [67.0-79.3]	125 (87.4) [80.8-92.4]	460 (79.2) [75.6-82.4]
False	8 (10.8)	16 (10.5)	36 (17.1)	13 (9.1)	73 (12.6)
I don't know	8 (10.8)	15 (9.8)	20 (9.5)	5 (3.5)	48 (8.3)
16b: Patients with depression					
True	2 (2.7)	8 (5.2)	21 (10.0)	18 (12.6)	49 (8.4)
False[a]	50 (67.6) [55.7-78.0]	122 (79.7) [72.5-85.8]	156 (73.9) [67.5-79.7]	101 (70.6) [62.4-77.9]	429 (73.8) [70.1-77.4]
I don't know	22 (29.7)	23 (15.0)	34 (16.1)	24 (16.8)	103 (17.7)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections					
True[a]	47 (63.5) [51.5-74.4]	115 (75.2) [67.5-81.8]	136 (64.5) [57.6-70.9]	123 (86.0) [79.2-91.2]	421 (72.5) [68.6-76.1]

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
False	15 (20.3)	21 (13.7)	53 (25.1)	13 (9.1)	102 (17.6)
I don't know	12 (16.2)	17 (11.1)	22 (10.4)	7 (4.9)	58 (10.0)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.					
17a: Major adverse cardiovascular events					
True[a]	59 (79.7) [68.8-88.2]	128 (83.7) [76.8-89.1]	166 (78.7) [72.5-84.0]	109 (76.2) [68.4-82.9]	462 (79.5) [76.0-82.7]
False	9 (12.2)	16 (10.5)	20 (9.5)	28 (19.6)	73 (12.6)
I don't know	6 (8.1)	9 (5.9)	25 (11.8)	6 (4.2)	46 (7.9)
17b: Venous thromboembolism					
True[a]	68 (91.9) [83.2-97.0]	145 (94.8) [90.0-97.7]	188 (89.1) [84.1-93.0]	131 (91.6) [85.8-95.6]	532 (91.6) [89.0-93.7]
False	3 (4.1)	6 (3.9)	9 (4.3)	8 (5.6)	26 (4.5)
I don't know	3 (4.1)	2 (1.3)	14 (6.6)	4 (2.8)	23 (4.0)
17c: Serious infections					
True[a]	24 (32.4) [22.0-44.3]	45 (29.4) [22.3-37.3]	64 (30.3) [24.2-37.0]	43 (30.1) [22.7-38.3]	176 (30.3) [26.6-34.2]
False	35 (47.3)	90 (58.8)	104 (49.3)	90 (62.9)	319 (54.9)

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
I don't know	15 (20.3)	18 (11.8)	43 (20.4)	10 (7.0)	86 (14.8)
17d: Mortality					
True[a]	16 (21.6) [12.9-32.7]	27 (17.6) [12.0-24.6]	44 (20.9) [15.6-27.0]	19 (13.3) [8.2-20.0]	106 (18.2) [15.2-21.6]
False	36 (48.6)	98 (64.1)	113 (53.6)	98 (68.5)	345 (59.4)
I don't know	22 (29.7)	28 (18.3)	54 (25.6)	26 (18.2)	130 (22.4)
Question 18: Which of the following statements is correct? *Select one only.*					
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	2 (2.7)	11 (7.2)	14 (6.6)	6 (4.2)	33 (5.7)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	44 (59.5) [47.4-70.7]	82 (53.6) [45.4-61.7]	132 (62.6) [55.7-69.1]	89 (62.2) [53.8-70.2]	347 (59.7) [55.6-63.7]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	6 (8.1)	13 (8.5)	14 (6.6)	9 (6.3)	42 (7.2)
I do not know	22 (29.7)	47 (30.7)	51 (24.2)	39 (27.3)	159 (27.4)

Table 3.1: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*					
Periodic skin examination[a]	53 (71.6) [59.9-81.5]	128 (83.7) [76.8-89.1]	170 (80.6) [74.6-85.7]	101 (70.6) [62.4-77.9]	452 (77.8) [74.2-81.1]
Periodic liver ultrasound	5 (6.8)	10 (6.5)	18 (8.5)	19 (13.3)	52 (9.0)
I do not know	16 (21.6)	15 (9.8)	23 (10.9)	23 (16.1)	77 (13.3)

Source: Appendix X, Table 3.1
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] Correct response.

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
Question 8: Which of the following statements is correct? *Select one only.*					
Olumiant (baricitinib) is contraindicated in pregnancy[a]	51 (68.9) [57.1-79.2]	123 (80.4) [73.2-86.4]	119 (74.4) [66.9-80.9]	94 (65.7) [57.3-73.5]	387 (73.0) [69.0-76.8]
Olumiant (baricitinib) is safe to use in pregnancy	0	1 (0.7)	2 (1.3)	4 (2.8)	7 (1.3)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	16 (21.6)	20 (13.1)	31 (19.4)	38 (26.6)	105 (19.8)
I do not know.	7 (9.5)	9 (5.9)	8 (5.0)	7 (4.9)	31 (5.8)
Question 9: Which of the following statements is correct? *Please select one option.*					
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	62 (83.8) [73.4-91.3]	138 (90.2) [84.3-94.4]	146 (91.3) [85.8-95.1]	133 (93.0) [87.5-96.6]	479 (90.4) [87.5-92.8]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	6 (8.1)	10 (6.5)	8 (5.0)	7 (4.9)	31 (5.8)
I do not know	6 (8.1)	5 (3.3)	6 (3.8)	3 (2.1)	20 (3.8)

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
Question 10: Which of the following statements is true? *Please select one option.*					
Olumiant (baricitinib) increases the potential risk of infection[a]	70 (94.6) [86.7-98.5]	147 (96.1) [91.7-98.5]	156 (97.5) [93.7-99.3]	134 (93.7) [88.4-97.1]	507 (95.7) [93.6-97.2]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	1 (1.4)	2 (1.3)	1 (0.6)	7 (4.9)	11 (2.1)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0	0	0	0	0
I do not know	3 (4.1)	4 (2.6)	3 (1.9)	2 (1.4)	12 (2.3)
Question 11: Which of the following statements is correct? *Select one only.*					
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	0	1 (0.7)	1 (0.6)	0	2 (0.4)
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	3 (4.1)	2 (1.3)	2 (1.3)	9 (6.3)	16 (3.0)

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	67 (90.5) [81.5-96.1]	148 (96.7) [92.5-98.9]	155 (96.9) [92.9-99.0]	132 (92.3) [86.7-96.1]	502 (94.7) [92.5-96.5]
I do not know	4 (5.4)	2 (1.3)	2 (1.3)	2 (1.4)	10 (1.9)
Question 12: Which of the following statements is correct? *Select one only.*					
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	52 (70.3) [58.5-80.3]	113 (73.9) [66.1-80.6]	125 (78.1) [70.9-84.3]	125 (87.4) [80.8-92.4]	415 (78.3) [74.5-81.7]
Olumiant (baricitinib) should never be used in patients over 65 of age	11 (14.9)	28 (18.3)	17 (10.6)	9 (6.3)	65 (12.3)
I do not know	11 (14.9)	12 (7.8)	18 (11.3)	9 (6.3)	50 (9.4)
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*					
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)					
True	7 (9.5)	14 (9.2)	21 (13.1)	17 (11.9)	59 (11.1)
False[a]	63 (85.1) [75.0-92.3]	132 (86.3) [79.8-91.3]	129 (80.6) [73.6-86.4]	120 (83.9) [76.9-89.5]	444 (83.8) [80.4-86.8]
I don't know	4 (5.4)	7 (4.6)	10 (6.3)	6 (4.2)	27 (5.1)

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors					
True[a]	68 (91.9) [83.2-97.0]	149 (97.4) [93.4-99.3]	158 (98.8) [95.6-99.8]	140 (97.9) [94.0-99.6]	515 (97.2) [95.4-98.4]
False	2 (2.7)	3 (2.0)	2 (1.3)	3 (2.1)	10 (1.9)
I don't know	4 (5.4)	1 (0.7)	0	0	5 (0.9)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism					
True[a]	73 (98.6) [92.7-100.0]	152 (99.3) [96.4-100.0]	160 (100.0) [97.7-100.0]	143 (100.0) [97.5-100.0]	528 (99.6) [98.6-100.0]
False	0	0	0	0	0
I don't know	1 (1.4)	1 (0.7)	0	0	2 (0.4)
Question 14: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***					
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)					
True[a]	64 (86.5) [76.5-93.3]	137 (89.5) [83.6-93.9]	149 (93.1) [88.0-96.5]	135 (94.4) [89.3-97.6]	485 (91.5) [88.8-93.7]
False	7 (9.5)	9 (5.9)	7 (4.4)	8 (5.6)	31 (5.8)
I don't know	3 (4.1)	7 (4.6)	4 (2.5)	0	14 (2.6)

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors					
True	21 (28.4)	52 (34.0)	46 (28.8)	35 (24.5)	154 (29.1)
False[a]	50 (67.6) [55.7-78.0]	94 (61.4) [53.2-69.2]	106 (66.3) [58.4-73.5]	104 (72.7) [64.7-79.8]	354 (66.8) [62.6-70.8]
I don't know	3 (4.1)	7 (4.6)	8 (5.0)	4 (2.8)	22 (4.2)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available					
True[a]	47 (63.5) [51.5-74.4]	136 (88.9) [82.8-93.4]	132 (82.5) [75.7-88.0]	94 (65.7) [57.3-73.5]	409 (77.2) [73.4-80.7]
False	18 (24.3)	9 (5.9)	18 (11.3)	44 (30.8)	89 (16.8)
I don't know	9 (12.2)	8 (5.2)	10 (6.3)	5 (3.5)	32 (6.0)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***					
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)					
True[a]	54 (73.0) [61.4-82.6]	104 (68.0) [60.0-75.3]	117 (73.1) [65.6-79.8]	105 (73.4) [65.4-80.5]	380 (71.7) [67.7-75.5]
False	9 (12.2)	29 (19.0)	22 (13.8)	16 (11.2)	76 (14.3)
I don't know	11 (14.9)	20 (13.1)	21 (13.1)	22 (15.4)	74 (14.0)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available					

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
True[a]	63 (85.1) [75.0-92.3]	138 (90.2) [84.3-94.4]	142 (88.8) [82.8-93.2]	125 (87.4) [80.8-92.4]	468 (88.3) [85.3-90.9]
False	5 (6.8)	7 (4.6)	8 (5.0)	14 (9.8)	34 (6.4)
I don't know	6 (8.1)	8 (5.2)	10 (6.3)	4 (2.8)	28 (5.3)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***					
16a: Patients aged 65 years or over					
True[a]	58 (78.4) [67.3-87.1]	122 (79.7) [72.5-85.8]	116 (72.5) [64.9-79.3]	125 (87.4) [80.8-92.4]	421 (79.4) [75.7-82.8]
False	8 (10.8)	16 (10.5)	28 (17.5)	13 (9.1)	65 (12.3)
I don't know	8 (10.8)	15 (9.8)	16 (10.0)	5 (3.5)	44 (8.3)
16b: Patients with depression					
True	2 (2.7)	8 (5.2)	16 (10.0)	18 (12.6)	44 (8.3)
False[a]	50 (67.6) [55.7-78.0]	122 (79.7) [72.5-85.8]	119 (74.4) [66.9-80.9]	101 (70.6) [62.4-77.9]	392 (74.0) [70.0-77.7]
I don't know	22 (29.7)	23 (15.0)	25 (15.6)	24 (16.8)	94 (17.7)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections					
True[a]	47 (63.5) [51.5-74.4]	115 (75.2) [67.5-81.8]	104 (65.0) [57.1-72.4]	123 (86.0) [79.2-91.2]	389 (73.4) [69.4-77.1]

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
False	15 (20.3)	21 (13.7)	37 (23.1)	13 (9.1)	86 (16.2)
I don't know	12 (16.2)	17 (11.1)	19 (11.9)	7 (4.9)	55 (10.4)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.					
17a: Major adverse cardiovascular events					
True[a]	59 (79.7) [68.8-88.2]	128 (83.7) [76.8-89.1]	131 (81.9) [75.0-87.5]	109 (76.2) [68.4-82.9]	427 (80.6) [76.9-83.9]
False	9 (12.2)	16 (10.5)	12 (7.5)	28 (19.6)	65 (12.3)
I don't know	6 (8.1)	9 (5.9)	17 (10.6)	6 (4.2)	38 (7.2)
17b: Venous thromboembolism					
True[a]	68 (91.9) [83.2-97.0]	145 (94.8) [90.0-97.7]	144 (90.0) [84.3-94.2]	131 (91.6) [85.8-95.6]	488 (92.1) [89.4-94.2]
False	3 (4.1)	6 (3.9)	8 (5.0)	8 (5.6)	25 (4.7)
I don't know	3 (4.1)	2 (1.3)	8 (5.0)	4 (2.8)	17 (3.2)
17c: Serious infections					
True[a]	24 (32.4) [22.0-44.3]	45 (29.4) [22.3-37.3]	43 (26.9) [20.2-34.4]	43 (30.1) [22.7-38.3]	155 (29.2) [25.4-33.3]
False	35 (47.3)	90 (58.8)	85 (53.1)	90 (62.9)	300 (56.6)

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
I don't know	15 (20.3)	18 (11.8)	32 (20.0)	10 (7.0)	75 (14.2)
17d: Mortality					
True[a]	16 (21.6) [12.9-32.7]	27 (17.6) [12.0-24.6]	36 (22.5) [16.3-29.8]	19 (13.3) [8.2-20.0]	98 (18.5) [15.3-22.1]
False	36 (48.6)	98 (64.1)	83 (51.9)	98 (68.5)	315 (59.4)
I don't know	22 (29.7)	28 (18.3)	41 (25.6)	26 (18.2)	117 (22.1)
Question 18: Which of the following statements is correct? *Select one only.*					
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	2 (2.7)	11 (7.2)	12 (7.5)	6 (4.2)	31 (5.8)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	44 (59.5) [47.4-70.7]	82 (53.6) [45.4-61.7]	106 (66.3) [58.4-73.5]	89 (62.2) [53.8-70.2]	321 (60.6) [56.3-64.8]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	6 (8.1)	13 (8.5)	10 (6.3)	9 (6.3)	38 (7.2)
I do not know	22 (29.7)	47 (30.7)	32 (20.0)	39 (27.3)	140 (26.4)
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*					

Table 3.1A: Responses to all Questions Related to the Understanding of the Important Safety Information by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
Periodic skin examination[a]	53 (71.6) [59.9-81.5]	128 (83.7) [76.8-89.1]	133 (83.1) [76.4-88.6]	101 (70.6) [62.4-77.9]	415 (78.3) [74.5-81.7]
Periodic liver ultrasound	5 (6.8)	10 (6.5)	10 (6.3)	19 (13.3)	44 (8.3)
I do not know	16 (21.6)	15 (9.8)	17 (10.6)	23 (16.1)	71 (13.4)

Source: Appendix X, Table 3.1A
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] Correct response.

Table 3.2: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Prescriber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
Question 8: Which of the following statements is correct? *Select one only.*		
Olumiant (baricitinib) is contraindicated in pregnancy[a]	368 (75.7) [71.7-79.5]	61 (64.2) [53.7-73.8]
Olumiant (baricitinib) is safe to use in pregnancy	6 (1.2)	1 (1.1)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	95 (19.5)	16 (16.8)
I do not know.	17 (3.5)	17 (17.9)
Question 9: Which of the following statements is correct? *Please select one option.*		
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	449 (92.4) [89.7-94.6]	72 (75.8) [65.9-84.0]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	26 (5.3)	11 (11.6)
I do not know	11 (2.3)	12 (12.6)
Question 10: Which of the following statements is true? *Please select one option.*		
Olumiant (baricitinib) increases the potential risk of infection[a]	469 (96.5) [94.5-97.9]	85 (89.5) [81.5-94.8]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	9 (1.9)	5 (5.3)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0	0
I do not know	8 (1.6)	5 (5.3)
Question 11: Which of the following statements is correct? *Select one only.*		
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	3 (0.6)	0
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	15 (3.1)	2 (2.1)

Table 3.2: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Prescriber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	464 (95.5) [93.2-97.1]	87 (91.6) [84.1-96.3]
I do not know	4 (0.8)	6 (6.3)
Question 12: Which of the following statements is correct? ***Select one only.***		
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	390 (80.2) [76.4-83.7]	65 (68.4) [58.1-77.6]
Olumiant (baricitinib) should never be used in patients over 65 of age	56 (11.5)	14 (14.7)
I do not know	40 (8.2)	16 (16.8)
Question 13: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)		
True	52 (10.7)	16 (16.8)
False[a]	409 (84.2) [80.6-87.3]	75 (78.9) [69.4-86.6]
I don't know	25 (5.1)	4 (4.2)
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors		
True[a]	473 (97.3) [95.5-98.6]	90 (94.7) [88.1-98.3]
False	10 (2.1)	2 (2.1)
I don't know	3 (0.6)	3 (3.2)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism		
True[a]	485 (99.8) [98.9-100.0]	94 (98.9) [94.3-100.0]
False	0	0
I don't know	1 (0.2)	1 (1.1)
Question 14: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		

Table 3.2: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Prescriber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)		
True[a]	450 (92.6) [89.9-94.8]	81 (85.3) [76.5-91.7]
False	26 (5.3)	6 (6.3)
I don't know	10 (2.1)	8 (8.4)
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors		
True	140 (28.8)	32 (33.7)
False[a]	331 (68.1) [63.8-72.2]	53 (55.8) [45.2-66.0]
I don't know	15 (3.1)	10 (10.5)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available		
True[a]	384 (79.0) [75.1-82.5]	61 (64.2) [53.7-73.8]
False	84 (17.3)	17 (17.9)
I don't know	18 (3.7)	17 (17.9)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)		
True[a]	357 (73.5) [69.3-77.3]	59 (62.1) [51.6-71.9]
False	71 (14.6)	13 (13.7)
I don't know	58 (11.9)	23 (24.2)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available		
True[a]	434 (89.3) [86.2-91.9]	76 (80.0) [70.5-87.5]
False	35 (7.2)	8 (8.4)
I don't know	17 (3.5)	11 (11.6)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***		

Table 3.2: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Prescriber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
16a: Patients aged 65 years or over		
True[a]	399 (82.1) [78.4-85.4]	61 (64.2) [53.7-73.8]
False	62 (12.8)	11 (11.6)
I don't know	25 (5.1)	23 (24.2)
16b: Patients with depression		
True	41 (8.4)	8 (8.4)
False[a]	370 (76.1) [72.1-79.9]	59 (62.1) [51.6-71.9]
I don't know	75 (15.4)	28 (29.5)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections		
True[a]	368 (75.7) [71.7-79.5]	53 (55.8) [45.2-66.0]
False	84 (17.3)	18 (18.9)
I don't know	34 (7.0)	24 (25.3)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.		
17a: Major adverse cardiovascular events		
True[a]	391 (80.5) [76.6-83.9]	71 (74.7) [64.8-83.1]
False	62 (12.8)	11 (11.6)
I don't know	33 (6.8)	13 (13.7)
17b: Venous thromboembolism		
True[a]	452 (93.0) [90.4-95.1]	80 (84.2) [75.3-90.9]
False	21 (4.3)	5 (5.3)
I don't know	13 (2.7)	10 (10.5)
17c: Serious infections		
True[a]	142 (29.2) [25.2-33.5]	34 (35.8) [26.2-46.3]
False	282 (58.0)	37 (38.9)

Table 3.2: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Prescriber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
I don't know	62 (12.8)	24 (25.3)
17d: Mortality		
True[a]	94 (19.3) [15.9-23.1]	12 (12.6) [6.7-21.0]
False	297 (61.1)	48 (50.5)
I don't know	95 (19.5)	35 (36.8)
Question 18: Which of the following statements is correct? *Select one only.*		
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	24 (4.9)	9 (9.5)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	301 (61.9) [57.5-66.3]	46 (48.4) [38.0-58.9]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	36 (7.4)	6 (6.3)
I do not know	125 (25.7)	34 (35.8)
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*		
Periodic skin examination[a]	384 (79.0) [75.1-82.5]	68 (71.6) [61.4-80.4]
Periodic liver ultrasound	41 (8.4)	11 (11.6)
I do not know	61 (12.6)	16 (16.8)

Source: Appendix X, Table 3.2
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] Correct response.

Table 3.3: Responses to all Questions Related to the Understanding of the Important Safety Information by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
Question 8: Which of the following statements is correct? *Select one only.*		
Olumiant (baricitinib) is contraindicated in pregnancy[a]	182 (73.4) [67.4-78.8]	247 (74.2) [69.1-78.8]
Olumiant (baricitinib) is safe to use in pregnancy	0	7 (2.1)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	58 (23.4)	53 (15.9)
I do not know.	8 (3.2)	26 (7.8)
Question 9: Which of the following statements is correct? *Please select one option.*		
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	233 (94.0) [90.2-96.6]	288 (86.5) [82.3-90.0]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	11 (4.4)	26 (7.8)
I do not know	4 (1.6)	19 (5.7)
Question 10: Which of the following statements is true? *Please select one option.*		
Olumiant (baricitinib) increases the potential risk of infection[a]	242 (97.6) [94.8-99.1]	312 (93.7) [90.5-96.1]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	2 (0.8)	12 (3.6)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0	0
I do not know	4 (1.6)	9 (2.7)
Question 11: Which of the following statements is correct? *Select one only.*		
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	0	3 (0.9)
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	3 (1.2)	14 (4.2)

Table 3.3: Responses to all Questions Related to the Understanding of the Important Safety Information by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	243 (98.0) [95.4-99.3]	308 (92.5) [89.1-95.1]
I do not know	2 (0.8)	8 (2.4)
Question 12: Which of the following statements is correct? *Select one only.*		
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	190 (76.6) [70.8-81.7]	265 (79.6) [74.8-83.8]
Olumiant (baricitinib) should never be used in patients over 65 of age	33 (13.3)	37 (11.1)
I do not know	25 (10.1)	31 (9.3)
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)		
True	22 (8.9)	46 (13.8)
False[a]	212 (85.5) [80.5-89.6]	272 (81.7) [77.1-85.7]
I don't know	14 (5.6)	15 (4.5)
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors		
True[a]	240 (96.8) [93.7-98.6]	323 (97.0) [94.5-98.6]
False	7 (2.8)	5 (1.5)
I don't know	1 (0.4)	5 (1.5)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism		
True[a]	247 (99.6) [97.8-100.0]	332 (99.7) [98.3-100.0]
False	0	0
I don't know	1 (0.4)	1 (0.3)
Question 14: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*		
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)		

Table 3.3: Responses to all Questions Related to the Understanding of the Important Safety Information by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
True[a]	234 (94.4) [90.7-96.9]	297 (89.2) [85.3-92.3]
False	10 (4.0)	22 (6.6)
I don't know	4 (1.6)	14 (4.2)
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors		
True	66 (26.6)	106 (31.8)
False[a]	174 (70.2) [64.0-75.8]	210 (63.1) [57.6-68.3]
I don't know	8 (3.2)	17 (5.1)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available		
True[a]	210 (84.7) [79.6-88.9]	235 (70.6) [65.4-75.4]
False	30 (12.1)	71 (21.3)
I don't know	8 (3.2)	27 (8.1)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)		
True[a]	190 (76.6) [70.8-81.7]	226 (67.9) [62.6-72.9]
False	33 (13.3)	51 (15.3)
I don't know	25 (10.1)	56 (16.8)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available		
True[a]	226 (91.1) [86.9-94.4]	284 (85.3) [81.0-88.9]
False	14 (5.6)	29 (8.7)
I don't know	8 (3.2)	20 (6.0)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***		
16a: Patients aged 65 years or over		
True[a]	197 (79.4) [73.9-84.3]	263 (79.0) [74.2-83.2]
False	40 (16.1)	33 (9.9)

Table 3.3: Responses to all Questions Related to the Understanding of the Important Safety Information by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
I don't know	11 (4.4)	37 (11.1)
16b: Patients with depression		
True	14 (5.6)	35 (10.5)
False[a]	202 (81.5) [76.0-86.1]	227 (68.2) [62.9-73.1]
I don't know	32 (12.9)	71 (21.3)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections		
True[a]	181 (73.0) [67.0-78.4]	240 (72.1) [66.9-76.8]
False	51 (20.6)	51 (15.3)
I don't know	16 (6.5)	42 (12.6)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.		
17a: Major adverse cardiovascular events		
True[a]	213 (85.9) [80.9-90.0]	249 (74.8) [69.8-79.4]
False	26 (10.5)	47 (14.1)
I don't know	9 (3.6)	37 (11.1)
17b: Venous thromboembolism		
True[a]	236 (95.2) [91.7-97.5]	296 (88.9) [85.0-92.1]
False	10 (4.0)	16 (4.8)
I don't know	2 (0.8)	21 (6.3)
17c: Serious infections		
True[a]	44 (17.7) [13.2-23.1]	132 (39.6) [34.3-45.1]
False	184 (74.2)	135 (40.5)
I don't know	20 (8.1)	66 (19.8)
17d: Mortality		
True[a]	41 (16.5) [12.1-21.8]	65 (19.5) [15.4-24.2]
False	172 (69.4)	173 (52.0)

Table 3.3: Responses to all Questions Related to the Understanding of the Important Safety Information by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
I don't know	35 (14.1)	95 (28.5)
Question 18: Which of the following statements is correct? *Select one only.*		
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	12 (4.8)	21 (6.3)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	170 (68.5) [62.4-74.3]	177 (53.2) [47.6-58.6]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	16 (6.5)	26 (7.8)
I do not know	50 (20.2)	109 (32.7)
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*		
Periodic skin examination[a]	186 (75.0) [69.1-80.3]	266 (79.9) [75.2-84.1]
Periodic liver ultrasound	23 (9.3)	29 (8.7)
I do not know	39 (15.7)	38 (11.4)

Source: Appendix X, Table 3.3
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] Correct response.

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
Question 8: Which of the following statements is correct? *Select one only.*		
Olumiant (baricitinib) is contraindicated in pregnancy[a]	207 (78.7) [73.3-83.5]	161 (72.2) [65.8-78.0]
Olumiant (baricitinib) is safe to use in pregnancy	4 (1.5)	2 (0.9)
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	42 (16.0)	53 (23.8)
I do not know.	10 (3.8)	7 (3.1)
Question 9: Which of the following statements is correct? *Please select one option.*		
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	239 (90.9) [86.7-94.1]	210 (94.2) [90.2-96.9]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	15 (5.7)	11 (4.9)
I do not know	9 (3.4)	2 (0.9)
Question 10: Which of the following statements is true? *Please select one option.*		
Olumiant (baricitinib) increases the potential risk of infection[a]	252 (95.8) [92.6-97.9]	217 (97.3) [94.2-99.0]

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	4 (1.5)	5 (2.2)
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0	0
I do not know	7 (2.7)	1 (0.4)
Question 11: Which of the following statements is correct? *Select one only.*		
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	2 (0.8)	1 (0.4)
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	9 (3.4)	6 (2.7)
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	249 (94.7) [91.2-97.1]	215 (96.4) [93.1-98.4]
I do not know	3 (1.1)	1 (0.4)
Question 12: Which of the following statements is correct? *Select one only.*		
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	205 (77.9) [72.4-82.8]	185 (83.0) [77.4-87.7]

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
Olumiant (baricitinib) should never be used in patients over 65 of age	38 (14.4)	18 (8.1)
I do not know	20 (7.6)	20 (9.0)
Question 13: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)		
True	26 (9.9)	26 (11.7)
False[a]	224 (85.2) [80.3-89.2]	185 (83.0) [77.4-87.7]
I don't know	13 (4.9)	12 (5.4)
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors		
True[a]	254 (96.6) [93.6-98.4]	219 (98.2) [95.5-99.5]
False	7 (2.7)	3 (1.3)
I don't know	2 (0.8)	1 (0.4)
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism		
True[a]	262 (99.6) [97.9-100.0]	223 (100.0) [98.4-100.0]
False	0	0
I don't know	1 (0.4)	0

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
Question 14: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)		
True[a]	245 (93.2) [89.4-95.9]	205 (91.9) [87.5-95.1]
False	12 (4.6)	14 (6.3)
I don't know	6 (2.3)	4 (1.8)
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors		
True	79 (30.0)	61 (27.4)
False[a]	172 (65.4) [59.3-71.1]	159 (71.3) [64.9-77.1]
I don't know	12 (4.6)	3 (1.3)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available		
True[a]	207 (78.7) [73.3-83.5]	177 (79.4) [73.5-84.5]
False	46 (17.5)	38 (17.0)
I don't know	10 (3.8)	8 (3.6)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***		
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)		
True[a]	186 (70.7) [64.8-76.2]	171 (76.7) [70.6-82.1]

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
False	40 (15.2)	31 (13.9)
I don't know	37 (14.1)	21 (9.4)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available		
True[a]	235 (89.4) [85.0-92.8]	199 (89.2) [84.4-93.0]
False	17 (6.5)	18 (8.1)
I don't know	11 (4.2)	6 (2.7)
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***		
16a: Patients aged 65 years or over		
True[a]	208 (79.1) [73.7-83.8]	191 (85.7) [80.4-90.0]
False	33 (12.5)	29 (13.0)
I don't know	22 (8.4)	3 (1.3)
16b: Patients with depression		
True	20 (7.6)	21 (9.4)
False[a]	192 (73.0) [67.2-78.3]	178 (79.8) [73.9-84.9]
I don't know	51 (19.4)	24 (10.8)

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections		
True[a]	191 (72.6) [66.8-77.9]	177 (79.4) [73.5-84.5]
False	47 (17.9)	37 (16.6)
I don't know	25 (9.5)	9 (4.0)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.		
17a: Major adverse cardiovascular events		
True[a]	209 (79.5) [74.1-84.2]	182 (81.6) [75.9-86.5]
False	34 (12.9)	28 (12.6)
I don't know	20 (7.6)	13 (5.8)
17b: Venous thromboembolism		
True[a]	240 (91.3) [87.2-94.4]	212 (95.1) [91.3-97.5]
False	15 (5.7)	6 (2.7)
I don't know	8 (3.0)	5 (2.2)
17c: Serious infections		
True[a]	76 (28.9) [23.5-34.8]	66 (29.6) [23.7-36.1]
False	144 (54.8)	138 (61.9)

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
I don't know	43 (16.3)	19 (8.5)
17d: Mortality		
True[a]	51 (19.4) [14.8-24.7]	43 (19.3) [14.3-25.1]
False	152 (57.8)	145 (65.0)
I don't know	60 (22.8)	35 (15.7)
Question 18: Which of the following statements is correct? *Select one only.*		
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	16 (6.1)	8 (3.6)
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	154 (58.6) [52.3-64.6]	147 (65.9) [59.3-72.1]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	22 (8.4)	14 (6.3)
I do not know	71 (27.0)	54 (24.2)
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*		
Periodic skin examination[a]	207 (78.7) [73.3-83.5]	177 (79.4) [73.5-84.5]
Periodic liver ultrasound	22 (8.4)	19 (8.5)

Table 3.4: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=263) n (%) [95% CI]	High Prescribers (N=223) n (%) [95% CI]
I do not know	34 (12.9)	27 (12.1)

Source: Appendix X, Table 3.4
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: Low prescribers: <= 5 patients in the last 6 months; High prescribers: => 6 patients in the last 6 months.
Note: This table does not include respondents who answered 'No' to Question 6: 'Have you prescribed Olumiant (baricitinib)?'.
[a] Correct response.

Table 3.5: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
Question 8: Which of the following statements is correct? *Select one only.*			
Olumiant (baricitinib) is contraindicated in pregnancy[a]	75 (68.2) [58.6-76.7]	346 (75.2) [71.0-79.1]	8 (72.7) [39.0-94.0]
Olumiant (baricitinib) is safe to use in pregnancy	1 (0.9)	6 (1.3)	0
Women of childbearing potential should use contraception during treatment with Olumiant (baricitinib) and for 6 months after the end of treatment	26 (23.6)	83 (18.0)	2 (18.2)
I do not know.	8 (7.3)	25 (5.4)	1 (9.1)
Question 9: Which of the following statements is correct? *Please select one option.*			
In patients taking Olumiant (baricitinib), lipid parameters should be monitored and hyperlipidaemia managed, if detected[a]	101 (91.8) [85.0-96.2]	411 (89.3) [86.2-92.0]	9 (81.8) [48.2-97.7]
There is no requirement to assess lipid parameters with Olumiant (baricitinib) dosing	7 (6.4)	28 (6.1)	2 (18.2)
I do not know	2 (1.8)	21 (4.6)	0
Question 10: Which of the following statements is true? *Please select one option.*			
Olumiant (baricitinib) increases the potential risk of infection[a]	104 (94.5) [88.5-98.0]	439 (95.4) [93.1-97.2]	11 (100.0) [71.5-100.0]
Patients can wait to mention any symptoms of infection at their next scheduled clinic visit	5 (4.5)	9 (2.0)	0
All patients taking Olumiant (baricitinib) should receive prophylactic antibiotics	0	0	0
I do not know	1 (0.9)	12 (2.6)	0
Question 11: Which of the following statements is correct? *Select one only.*			

Table 3.5: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
If Herpes Zoster or any other infection does not respond to standard treatment, Olumiant (baricitinib) can be continued	1 (0.9)	2 (0.4)	0
Patients can be immunised with live attenuated vaccines shortly before or during treatment with Olumiant (baricitinib)	2 (1.8)	14 (3.0)	1 (9.1)
Patients should be screened for viral hepatitis and active tuberculosis should be ruled out before commencing Olumiant (baricitinib) therapy[a]	106 (96.4) [91.0-99.0]	435 (94.6) [92.1-96.5]	10 (90.9) [58.7-99.8]
I do not know	1 (0.9)	9 (2.0)	0
Question 12: Which of the following statements is correct? *Select one only.*			
Caution should be used when treating patients with diabetes with Olumiant (baricitinib)[a]	89 (80.9) [72.3-87.8]	357 (77.6) [73.5-81.3]	9 (81.8) [48.2-97.7]
Olumiant (baricitinib) should never be used in patients over 65 of age	10 (9.1)	59 (12.8)	1 (9.1)
I do not know	11 (10.0)	44 (9.6)	1 (9.1)
Question 13: *Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).*			
13a: There is no increased risk of venous thrombosis or pulmonary embolism in patients receiving Olumiant (baricitinib)			
True	20 (18.2)	48 (10.4)	0
False[a]	85 (77.3) [68.3-84.7]	389 (84.6) [80.9-87.7]	10 (90.9) [58.7-99.8]
I don't know	5 (4.5)	23 (5.0)	1 (9.1)
13b: Olumiant (baricitinib) should be used with caution in patients with risk factors for deep vein thrombosis/pulmonary embolism other than cardiovascular or malignancy risk factors			
True[a]	105 (95.5) [89.7-98.5]	447 (97.2) [95.2-98.5]	11 (100.0) [71.5-100.0]
False	5 (4.5)	7 (1.5)	0

Table 3.5: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
I don't know	0	6 (1.3)	0
13c: Patients should be advised to seek immediate medical attention if they develop signs or symptoms of deep vein thrombosis/pulmonary embolism			
True[a]	110 (100.0) [96.7-100.0]	458 (99.6) [98.4-99.9]	11 (100.0) [71.5-100.0]
False	0	0	0
I don't know	0	2 (0.4)	0
Question 14: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***			
14a: There is a potentially increased risk of major adverse cardiovascular events in patients with certain risk factors using JAK inhibitor treatment including Olumiant (baricitinib)			
True[a]	100 (90.9) [83.9-95.6]	421 (91.5) [88.6-93.9]	10 (90.9) [58.7-99.8]
False	6 (5.5)	26 (5.7)	0
I don't know	4 (3.6)	13 (2.8)	1 (9.1)
14b: Olumiant (baricitinib) is contraindicated in patients with cardiovascular risk factors			
True	36 (32.7)	134 (29.1)	2 (18.2)
False[a]	70 (63.6) [53.9-72.6]	306 (66.5) [62.0-70.8]	8 (72.7) [39.0-94.0]
I don't know	4 (3.6)	20 (4.3)	1 (9.1)
14c: In patients who are past or current smokers, Olumiant (baricitinib) should only be used if no suitable treatment alternatives are available			
True[a]	86 (78.2) [69.3-85.5]	351 (76.3) [72.1-80.1]	8 (72.7) [39.0-94.0]
False	19 (17.3)	81 (17.6)	1 (9.1)
I don't know	5 (4.5)	28 (6.1)	2 (18.2)
Question 15: ***Please answer True, False, or I do not know for each of the following statements regarding Olumiant (baricitinib).***			
15a: Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, including Olumiant (baricitinib)			
True[a]	82 (74.5) [65.4-82.4]	326 (70.9) [66.5-75.0]	8 (72.7) [39.0-94.0]
False	14 (12.7)	70 (15.2)	0

Table 3.5: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
I don't know	14 (12.7)	64 (13.9)	3 (27.3)
15b: In patients with a past history of malignancy or with other malignancy risk factors Olumiant (baricitinib) should only be used if no suitable alternative treatments are available			
True[a]	95 (86.4) [78.5-92.2]	405 (88.0) [84.7-90.9]	10 (90.9) [58.7-99.8]
False	12 (10.9)	30 (6.5)	1 (9.1)
I don't know	3 (2.7)	25 (5.4)	0
Question 16: For which patients is a 2mg once daily dose recommended. ***Please answer True, False, or I do not know for each statement.***			
16a: Patients aged 65 years or over			
True[a]	90 (81.8) [73.3-88.5]	362 (78.7) [74.7-82.4]	8 (72.7) [39.0-94.0]
False	15 (13.6)	57 (12.4)	1 (9.1)
I don't know	5 (4.5)	41 (8.9)	2 (18.2)
16b: Patients with depression			
True	10 (9.1)	39 (8.5)	0
False[a]	84 (76.4) [67.3-83.9]	338 (73.5) [69.2-77.5]	7 (63.6) [30.8-89.1]
I don't know	16 (14.5)	83 (18.0)	4 (36.4)
16c: Patients at a higher risk of malignancy, venous thromboembolism and major adverse cardiovascular events or with a history of chronic or recurrent infections			
True[a]	84 (76.4) [67.3-83.9]	329 (71.5) [67.2-75.6]	8 (72.7) [39.0-94.0]
False	18 (16.4)	83 (18.0)	1 (9.1)
I don't know	8 (7.3)	48 (10.4)	2 (18.2)
Question 17: An increased incidence of which of the following have been observed with JAK inhibitor treatment compared to Tumour Necrosis Factor α (TNFα) inhibitors? Please answer True, False, or I do not know for each statement.			
17a: Major adverse cardiovascular events			
True[a]	89 (80.9) [72.3-87.8]	365 (79.3) [75.4-83.0]	8 (72.7) [39.0-94.0]
False	15 (13.6)	56 (12.2)	2 (18.2)
I don't know	6 (5.5)	39 (8.5)	1 (9.1)

Table 3.5: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
17b: Venous thromboembolism			
True[a]	104 (94.5) [88.5-98.0]	418 (90.9) [87.9-93.3]	10 (90.9) [58.7-99.8]
False	5 (4.5)	21 (4.6)	0
I don't know	1 (0.9)	21 (4.6)	1 (9.1)
17c: Serious infections			
True[a]	30 (27.3) [19.2-36.6]	140 (30.4) [26.3-34.9]	6 (54.5) [23.4-83.3]
False	70 (63.6)	245 (53.3)	4 (36.4)
I don't know	10 (9.1)	75 (16.3)	1 (9.1)
17d: Mortality			
True[a]	21 (19.1) [12.2-27.7]	83 (18.0) [14.6-21.9]	2 (18.2) [2.3-51.8]
False	71 (64.5)	267 (58.0)	7 (63.6)
I don't know	18 (16.4)	110 (23.9)	2 (18.2)
Question 18: Which of the following statements is correct? *Select one only.*			
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of depression	5 (4.5)	28 (6.1)	0
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of malignancy[a]	64 (58.2) [48.4-67.5]	275 (59.8) [55.1-64.3]	8 (72.7) [39.0-94.0]
Compared with TNFα inhibitors, JAK inhibitor treatment has been associated with an increased incidence of diabetes	7 (6.4)	34 (7.4)	1 (9.1)
I do not know	34 (30.9)	123 (26.7)	2 (18.2)
Question 19: Which of the following is recommended for patients treated with Olumiant (baricitinib)? *Select one only.*			
Periodic skin examination[a]	88 (80.0) [71.3-87.0]	358 (77.8) [73.7-81.5]	6 (54.5) [23.4-83.3]
Periodic liver ultrasound	7 (6.4)	42 (9.1)	3 (27.3)

Table 3.5: Responses to all Questions Related to the Understanding of the Important Safety Information by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%) [95% CI]	Medium (N=460) n (%) [95% CI]	Low (N=11) n (%) [95% CI]
I do not know	15 (13.6)	60 (13.0)	2 (18.2)

Source: Appendix X, Table 3.5
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: High experience will be defined as prescriber with >15 years experience and more than 25 RA/Dermatology patients. Low experience will be defined as prescribers with <5 years experience and less than 5 RA/Dermatology patients. All other prescribers will be counted as Medium experience including those with experience missing.
[a] Correct response.

Table 4: Understanding the Key Risk Messages for Objective 1 - Completed Surveys

	Respondents (N=530) n (%) [95% CI]
KRM#1 Pregnancy (Q8)[a]	
Yes	387 (73.0) [69.0-76.8]
No	143 (27.0)
KRM#2 Lipid parameters (Q9)[b]	
Yes	479 (90.4) [87.5-92.8]
No	51 (9.6)
KRM#3 Infections (Q10, Q11, Q12)[c]	
Yes	389 (73.4) [69.4-77.1]
No	141 (26.6)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]	
Yes	434 (81.9) [78.3-85.1]
No	96 (18.1)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]	
Yes	254 (47.9) [43.6-52.3]
No	276 (52.1)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]	
Yes	350 (66.0) [61.8-70.1]
No	180 (34.0)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]	
Yes	280 (52.8) [48.5-57.1]
No	250 (47.2)
Understanding all KRMs for Objective 1	
Yes	76 (14.3) [11.5-17.6]

Table 4: Understanding the Key Risk Messages for Objective 1 - Completed Surveys

	Respondents (N=530) n (%) [95% CI]
No	454 (85.7)

Source: Appendix X, Table 4
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 4.1: Understanding the Key Risk Messages for Objective 1 by Country - Completed Surveys Including all Dermatologists from Germany

	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
KRM#1 Pregnancy (Q8)[a]					
Yes	51 (68.9) [57.1-79.2]	123 (80.4) [73.2-86.4]	161 (76.3) [70.0-81.9]	94 (65.7) [57.3-73.5]	429 (73.8) [70.1-77.4]
No	23 (31.1)	30 (19.6)	50 (23.7)	49 (34.3)	152 (26.2)
KRM#2 Lipid parameters (Q9)[b]					
Yes	62 (83.8) [73.4-91.3]	138 (90.2) [84.3-94.4]	188 (89.1) [84.1-93.0]	133 (93.0) [87.5-96.6]	521 (89.7) [86.9-92.0]
No	12 (16.2)	15 (9.8)	23 (10.9)	10 (7.0)	60 (10.3)
KRM#3 Infections (Q10, Q11, Q12)[c]					
Yes	47 (63.5) [51.5-74.4]	109 (71.2) [63.4-78.3]	160 (75.8) [69.5-81.4]	110 (76.9) [69.1-83.6]	426 (73.3) [69.5-76.9]
No	27 (36.5)	44 (28.8)	51 (24.2)	33 (23.1)	155 (26.7)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]					
Yes	60 (81.1) [70.3-89.3]	129 (84.3) [77.6-89.7]	167 (79.1) [73.0-84.4]	117 (81.8) [74.5-87.8]	473 (81.4) [78.0-84.5]
No	14 (18.9)	24 (15.7)	44 (20.9)	26 (18.2)	108 (18.6)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]					
Yes	31 (41.9) [30.5-53.9]	77 (50.3) [42.1-58.5]	107 (50.7) [43.8-57.6]	60 (42.0) [33.8-50.5]	275 (47.3) [43.2-51.5]
No	43 (58.1)	76 (49.7)	104 (49.3)	83 (58.0)	306 (52.7)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]					
Yes	47 (63.5) [51.5-74.4]	98 (64.1) [55.9-71.6]	142 (67.3) [60.5-73.6]	95 (66.4) [58.1-74.1]	382 (65.7) [61.7-69.6]
No	27 (36.5)	55 (35.9)	69 (32.7)	48 (33.6)	199 (34.3)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]					
Yes	32 (43.2) [31.8-55.3]	91 (59.5) [51.3-67.3]	99 (46.9) [40.0-53.9]	79 (55.2) [46.7-63.6]	301 (51.8) [47.7-55.9]
No	42 (56.8)	62 (40.5)	112 (53.1)	64 (44.8)	280 (48.2)
Understanding all KRMs for Objective 1					

Table 4.1: Understanding the Key Risk Messages for Objective 1 by Country - Completed Surveys Including all Dermatologists from Germany

	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
Yes	7 (9.5) [3.9-18.5]	23 (15.0) [9.8-21.7]	33 (15.6) [11.0-21.3]	20 (14.0) [8.8-20.8]	83 (14.3) [11.5-17.4]
No	67 (90.5)	130 (85.0)	178 (84.4)	123 (86.0)	498 (85.7)

Source: Appendix X, Table 4.1
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 4.1A: Understanding the Key Risk Messages for Objective 1 by Country - Completed Surveys

	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
KRM#1 Pregnancy (Q8)[a]					
Yes	51 (68.9) [57.1-79.2]	123 (80.4) [73.2-86.4]	119 (74.4) [66.9-80.9]	94 (65.7) [57.3-73.5]	387 (73.0) [69.0-76.8]
No	23 (31.1)	30 (19.6)	41 (25.6)	49 (34.3)	143 (27.0)
KRM#2 Lipid parameters (Q9)[b]					
Yes	62 (83.8) [73.4-91.3]	138 (90.2) [84.3-94.4]	146 (91.3) [85.8-95.1]	133 (93.0) [87.5-96.6]	479 (90.4) [87.5-92.8]
No	12 (16.2)	15 (9.8)	14 (8.8)	10 (7.0)	51 (9.6)
KRM#3 Infections (Q10, Q11, Q12)[c]					
Yes	47 (63.5) [51.5-74.4]	109 (71.2) [63.4-78.3]	123 (76.9) [69.6-83.2]	110 (76.9) [69.1-83.6]	389 (73.4) [69.4-77.1]
No	27 (36.5)	44 (28.8)	37 (23.1)	33 (23.1)	141 (26.6)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]					
Yes	60 (81.1) [70.3-89.3]	129 (84.3) [77.6-89.7]	128 (80.0) [73.0-85.9]	117 (81.8) [74.5-87.8]	434 (81.9) [78.3-85.1]
No	14 (18.9)	24 (15.7)	32 (20.0)	26 (18.2)	96 (18.1)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]					
Yes	31 (41.9) [30.5-53.9]	77 (50.3) [42.1-58.5]	86 (53.8) [45.7-61.7]	60 (42.0) [33.8-50.5]	254 (47.9) [43.6-52.3]
No	43 (58.1)	76 (49.7)	74 (46.3)	83 (58.0)	276 (52.1)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]					
Yes	47 (63.5) [51.5-74.4]	98 (64.1) [55.9-71.6]	110 (68.8) [61.0-75.8]	95 (66.4) [58.1-74.1]	350 (66.0) [61.8-70.1]
No	27 (36.5)	55 (35.9)	50 (31.3)	48 (33.6)	180 (34.0)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]					
Yes	32 (43.2) [31.8-55.3]	91 (59.5) [51.3-67.3]	78 (48.8) [40.8-56.8]	79 (55.2) [46.7-63.6]	280 (52.8) [48.5-57.1]
No	42 (56.8)	62 (40.5)	82 (51.3)	64 (44.8)	250 (47.2)
Understanding all KRMs for Objective 1					

Table 4.1A: Understanding the Key Risk Messages for Objective 1 by Country - Completed Surveys

	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
Yes	7 (9.5) [3.9-18.5]	23 (15.0) [9.8-21.7]	26 (16.3) [10.9-22.9]	20 (14.0) [8.8-20.8]	76 (14.3) [11.5-17.6]
No	67 (90.5)	130 (85.0)	134 (83.8)	123 (86.0)	454 (85.7)

Source: Appendix X, Table 4.1A
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 4.2: Understanding the Key Risk Messages for Objective 1 by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

	Prescribing Status	
	Active Presciber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
KRM#1 Pregnancy (Q8)[a]		
Yes	368 (75.7) [71.7-79.5]	61 (64.2) [53.7-73.8]
No	118 (24.3)	34 (35.8)
KRM#2 Lipid parameters (Q9)[b]		
Yes	449 (92.4) [89.7-94.6]	72 (75.8) [65.9-84.0]
No	37 (7.6)	23 (24.2)
KRM#3 Infections (Q10, Q11, Q12)[c]		
Yes	368 (75.7) [71.7-79.5]	58 (61.1) [50.5-70.9]
No	118 (24.3)	37 (38.9)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]		
Yes	400 (82.3) [78.6-85.6]	73 (76.8) [67.1-84.9]
No	86 (17.7)	22 (23.2)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]		
Yes	239 (49.2) [44.6-53.7]	36 (37.9) [28.1-48.4]
No	247 (50.8)	59 (62.1)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]		
Yes	331 (68.1) [63.8-72.2]	51 (53.7) [43.2-64.0]
No	155 (31.9)	44 (46.3)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]		
Yes	265 (54.5) [50.0-59.0]	36 (37.9) [28.1-48.4]
No	221 (45.5)	59 (62.1)
Understanding all KRMs for Objective 1		

Table 4.2: Understanding the Key Risk Messages for Objective 1 by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

	Prescribing Status	
	Active Presciber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
Yes	75 (15.4) [12.3-19.0]	8 (8.4) [3.7-15.9]
No	411 (84.6)	87 (91.6)

Source: Appendix X, Table 4.2
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 4.3: Understanding the Key Risk Messages for Objective 1 by Specialty - Completed Surveys Including all Dermatologists from Germany

	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
KRM#1 Pregnancy (Q8)[a]		
Yes	182 (73.4) [67.4-78.8]	247 (74.2) [69.1-78.8]
No	66 (26.6)	86 (25.8)
KRM#2 Lipid parameters (Q9)[b]		
Yes	233 (94.0) [90.2-96.6]	288 (86.5) [82.3-90.0]
No	15 (6.0)	45 (13.5)
KRM#3 Infections (Q10, Q11, Q12)[c]		
Yes	186 (75.0) [69.1-80.3]	240 (72.1) [66.9-76.8]
No	62 (25.0)	93 (27.9)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]		
Yes	205 (82.7) [77.4-87.2]	268 (80.5) [75.8-84.6]
No	43 (17.3)	65 (19.5)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]		
Yes	136 (54.8) [48.4-61.1]	139 (41.7) [36.4-47.2]
No	112 (45.2)	194 (58.3)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]		
Yes	175 (70.6) [64.5-76.2]	207 (62.2) [56.7-67.4]
No	73 (29.4)	126 (37.8)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]		
Yes	135 (54.4) [48.0-60.7]	166 (49.8) [44.4-55.4]
No	113 (45.6)	167 (50.2)
Understanding all KRMs for Objective 1		

Table 4.3: Understanding the Key Risk Messages for Objective 1 by Specialty - Completed Surveys Including all Dermatologists from Germany

	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
Yes	32 (12.9) [9.0-17.7]	51 (15.3) [11.6-19.6]
No	216 (87.1)	282 (84.7)

Source: Appendix X, Table 4.3
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 4.4: Understanding the Key Risk Messages for Objective 1 by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

	Prescribing Frequency	
	Low Prescibers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
KRM#1 Pregnancy (Q8)[a]		
Yes	207 (78.7) [73.3-83.5]	161 (72.2) [65.8-78.0]
No	56 (21.3)	62 (27.8)
KRM#2 Lipid parameters (Q9)[b]		
Yes	239 (90.9) [86.7-94.1]	210 (94.2) [90.2-96.9]
No	24 (9.1)	13 (5.8)
KRM#3 Infections (Q10, Q11, Q12)[c]		
Yes	191 (72.6) [66.8-77.9]	177 (79.4) [73.5-84.5]
No	72 (27.4)	46 (20.6)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]		
Yes	218 (82.9) [77.8-87.2]	182 (81.6) [75.9-86.5]
No	45 (17.1)	41 (18.4)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]		
Yes	130 (49.4) [43.2-55.6]	109 (48.9) [42.1-55.6]
No	133 (50.6)	114 (51.1)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]		
Yes	172 (65.4) [59.3-71.1]	159 (71.3) [64.9-77.1]
No	91 (34.6)	64 (28.7)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]		
Yes	130 (49.4) [43.2-55.6]	135 (60.5) [53.8-67.0]
No	133 (50.6)	88 (39.5)
Understanding all KRMs for Objective 1		

Table 4.4: Understanding the Key Risk Messages for Objective 1 by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

	Prescribing Frequency	
	Low Prescibers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
Yes	38 (14.4) [10.4-19.3]	37 (16.6) [12.0-22.1]
No	225 (85.6)	186 (83.4)

Source: Appendix X, Table 4.4
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: Low prescribers: <= 5 patients in the last 6 months; High prescribers: => 6 patients in the last 6 months.
Note: This table does not include respondents who answered 'No' to Question 6: 'Have you prescribed Olumiant (baricitinib)?'.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 4.5: Understanding the Key Risk Messages for Objective 1 by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
KRM#1 Pregnancy (Q8)[a]			
Yes	75 (68.2) [58.6-76.7]	346 (75.2) [71.0-79.1]	8 (72.7) [39.0-94.0]
No	35 (31.8)	114 (24.8)	3 (27.3)
KRM#2 Lipid parameters (Q9)[b]			
Yes	101 (91.8) [85.0-96.2]	411 (89.3) [86.2-92.0]	9 (81.8) [48.2-97.7]
No	9 (8.2)	49 (10.7)	2 (18.2)
KRM#3 Infections (Q10, Q11, Q12)[c]			
Yes	84 (76.4) [67.3-83.9]	334 (72.6) [68.3-76.6]	8 (72.7) [39.0-94.0]
No	26 (23.6)	126 (27.4)	3 (27.3)
KRM#4 Venous thromboembolism (Q13a, Q13b, Q13c)[d]			
Yes	82 (74.5) [65.4-82.4]	381 (82.8) [79.1-86.2]	10 (90.9) [58.7-99.8]
No	28 (25.5)	79 (17.2)	1 (9.1)
KRM#5 Major Adverse Cardiovascular Events (Q14a, Q14b, Q14c)[e]			
Yes	47 (42.7) [33.3-52.5]	222 (48.3) [43.6-52.9]	6 (54.5) [23.4-83.3]
No	63 (57.3)	238 (51.7)	5 (45.5)
KRM#6 Lymphoma and other Malignancies (Q15a, Q15b)[f]			
Yes	76 (69.1) [59.6-77.6]	299 (65.0) [60.4-69.4]	7 (63.6) [30.8-89.1]
No	34 (30.9)	161 (35.0)	4 (36.4)
KRM#7 Dosing (Q16a, Q16b, Q16c)[g]			
Yes	62 (56.4) [46.6-65.8]	233 (50.7) [46.0-55.3]	6 (54.5) [23.4-83.3]
No	48 (43.6)	227 (49.3)	5 (45.5)
Understanding all KRMs for Objective 1			

Table 4.5: Understanding the Key Risk Messages for Objective 1 by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
Yes	14 (12.7) [7.1-20.4]	68 (14.8) [11.7-18.4]	1 (9.1) [0.2-41.3]
No	96 (87.3)	392 (85.2)	10 (90.9)

Source: Appendix X, Table 4.5
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: High experience will be defined as prescriber with >15 years experience and more than 25 RA/Dermatology patients. Low experience will be defined as prescribers with <5 years experience and less than 5 RA/Dermatology patients. All other prescribers will be counted as Medium experience including those with experience missing.
[a] To be counted as understanding of KRM#1, Q8 must be answered correctly.
[b] To be counted as understanding of KRM#2, Q9 must be answered correctly.
[c] To be counted as understanding of KRM#3, Q10, Q11, and Q12 must be answered correctly.
[d] To be counted as understanding of KRM#4, Q13a, Q13b, and Q13c must be answered correctly.
[e] To be counted as understanding of KRM#5, Q14a, Q14b, and Q14c must be answered correctly.
[f] To be counted as understanding of KRM#6, Q15a and Q15b must be answered correctly.
[g] To be counted as understanding of KRM#7, Q16a, Q16b and Q16c must be answered correctly.

Table 5: Understanding the Key Risk Messages for Objective 2 - Completed Surveys

	Respondents (N=530) n (%) [95% CI]
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]	
Yes	40 (7.5) [5.4-10.1]
No	490 (92.5)

Source: Appendix X, Table 5
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 5.1: Understanding the Key Risk Messages for Objective 2 by Country - Completed Surveys Including all Dermatologists from Germany

	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=211) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=581) n (%) [95% CI]**
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]					
Yes	7 (9.5) [3.9-18.5]	13 (8.5) [4.6-14.1]	18 (8.5) [5.1-13.1]	5 (3.5) [1.1-8.0]	43 (7.4) [5.4-9.8]
No	67 (90.5)	140 (91.5)	193 (91.5)	138 (96.5)	538 (92.6)

Source: Appendix X, Table 5.1
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 5.1A: Understanding the Key Risk Messages for Objective 2 by Country - Completed Surveys

	Country				
	Sweden (N=74) n (%) [95% CI]	**France (N=153) n (%) [95% CI]**	**Germany (N=160) n (%) [95% CI]**	**Spain (N=143) n (%) [95% CI]**	**Overall (N=530) n (%) [95% CI]**
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]					
Yes	7 (9.5) [3.9-18.5]	13 (8.5) [4.6-14.1]	15 (9.4) [5.3-15.0]	5 (3.5) [1.1-8.0]	40 (7.5) [5.4-10.1]
No	67 (90.5)	140 (91.5)	145 (90.6)	138 (96.5)	490 (92.5)

Source: Appendix X, Table 5.1A
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 5.2: Understanding the Key Risk Messages for Objective 2 by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

	Prescribing Status	
	Active Presciber (N=486) n (%) [95% CI]	**Potential Prescribers (N=95) n (%) [95% CI]**
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]		
Yes	37 (7.6) [5.4-10.3]	6 (6.3) [2.4-13.2]
No	449 (92.4)	89 (93.7)

Source: Appendix X, Table 5.2
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 5.3: Understanding the Key Risk Messages for Objective 2 by Specialty - Completed Surveys Including all Dermatologists from Germany

	Specialty	
	Rheumatologist (N=248) n (%) [95% CI]	**Dermatologist (N=333) n (%) [95% CI]**
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]		
Yes	14 (5.6) [3.1-9.3]	29 (8.7) [5.9-12.3]
No	234 (94.4)	304 (91.3)

Source: Appendix X, Table 5.3
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 5.4: Understanding the Key Risk Messages for Objective 2 by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

	Prescribing Frequency	
	Low Prescibers (N=263) n (%) [95% CI]	**High Prescribers (N=223) n (%) [95% CI]**
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]		
Yes	18 (6.8) [4.1-10.6]	19 (8.5) [5.2-13.0]
No	245 (93.2)	204 (91.5)

Source: Appendix X, Table 5.4
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: Low prescribers: <= 5 patients in the last 6 months; High prescribers: => 6 patients in the last 6 months.
Note: This table does not include respondents who answered 'No' to Question 6: 'Have you prescribed Olumiant (baricitinib)?'.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 5.5: Understanding the Key Risk Messages for Objective 2 by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

	Prescriber Experience		
	High (N=110) n (%) [95% CI]	**Medium (N=460) n (%) [95% CI]**	**Low (N=11) n (%) [95% CI]**
KRM#8 JAK inhibitor class effect (Q17a, Q17b, Q17c, Q17d, Q18, and Q19)[a]			
Yes	12 (10.9) [5.8-18.3]	29 (6.3) [4.3-8.9]	2 (18.2) [2.3-51.8]
No	98 (89.1)	431 (93.7)	9 (81.8)

Source: Appendix X, Table 5.5
Note: 95% exact two-sided confidence intervals are calculated using the Clopper-Pearson method.
Note: High experience will be defined as prescriber with >15 years experience and more than 25 RA/Dermatology patients. Low experience will be defined as prescribers with <5 years experience and less than 5 RA/Dermatology patients. All other prescribers will be counted as Medium experience including those with experience missing.
[a] To be counted as understanding of KRM#8, Q17a, Q17b, Q17c, Q17d, Q18, and Q19 must be answered correctly.

Table 6: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) - Completed Surveys

Question	Respondents (N=530) n (%)
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?	
Yes	276 (52.1)
No	254 (47.9)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]	
Yes	168 (60.9)
No	44 (15.9)
I don't remember	64 (23.2)
N/A (Answered "No" to Question 20)	254
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]	
Yes	127 (75.6)
No	23 (13.7)
I don't remember	18 (10.7)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	362
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?	
Yes	277 (52.3)
No	253 (47.7)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]	
Yes	176 (92.6)
No	12 (6.3)
I don't know	2 (1.1)
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	340
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]	
Yes	15 (8.5)
No	141 (80.1)
I don't know	20 (11.4)

Table 6: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) - Completed Surveys

Question	Respondents (N=530) n (%)
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	354
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?	
Yes	366 (69.1)
No	81 (15.3)
I don't know	83 (15.7)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]	
Yes	325 (88.8)
No	29 (7.9)
I don't know	12 (3.3)
N/A (Answered "No" or "I don't know" to Question 26)	164

Source: Appendix X, Table 6
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 6.1: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%)	France (N=153) n (%)	Germany (N=211) n (%)	Spain (N=143) n (%)	Overall (N=581) n (%)
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?					
Yes	38 (51.4)	101 (66.0)	80 (37.9)	74 (51.7)	293 (50.4)
No	36 (48.6)	52 (34.0)	131 (62.1)	69 (48.3)	288 (49.6)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]					
Yes	20 (52.6)	67 (66.3)	61 (76.3)	35 (47.3)	183 (62.5)
No	6 (15.8)	15 (14.9)	8 (10.0)	16 (21.6)	45 (15.4)
I don't remember	12 (31.6)	19 (18.8)	11 (13.8)	23 (31.1)	65 (22.2)
N/A (Answered "No" to Question 20)	36	52	131	69	288
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]					
Yes	17 (85.0)	48 (71.6)	45 (73.8)	29 (82.9)	139 (76.0)
No	0	13 (19.4)	8 (13.1)	3 (8.6)	24 (13.1)
I don't remember	3 (15.0)	6 (9.0)	8 (13.1)	3 (8.6)	20 (10.9)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	54	86	150	108	398
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?					
Yes	32 (43.2)	85 (55.6)	115 (54.5)	68 (47.6)	300 (51.6)
No	42 (56.8)	68 (44.4)	96 (45.5)	75 (52.4)	281 (48.4)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]					
Yes	25 (89.3)	42 (91.3)	70 (94.6)	60 (92.3)	197 (92.5)
No	2 (7.1)	3 (6.5)	4 (5.4)	5 (7.7)	14 (6.6)
I don't know	1 (3.6)	1 (2.2)	0	0	2 (0.9)
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	46	107	137	78	368

Table 6.1: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Country - Completed Surveys Including all Dermatologists from Germany

Question	Country				
	Sweden (N=74) n (%)	France (N=153) n (%)	Germany (N=211) n (%)	Spain (N=143) n (%)	Overall (N=581) n (%)
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]					
Yes	5 (20.0)	5 (11.9)	7 (10.0)	1 (1.7)	18 (9.1)
No	10 (40.0)	37 (88.1)	58 (82.9)	54 (90.0)	159 (80.7)
I don't know	10 (40.0)	0	5 (7.1)	5 (8.3)	20 (10.2)
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	49	111	141	83	384
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?					
Yes	36 (48.6)	116 (75.8)	181 (85.8)	77 (53.8)	410 (70.6)
No	14 (18.9)	17 (11.1)	16 (7.6)	38 (26.6)	85 (14.6)
I don't know	24 (32.4)	20 (13.1)	14 (6.6)	28 (19.6)	86 (14.8)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]					
Yes	30 (83.3)	102 (87.9)	163 (90.1)	69 (89.6)	364 (88.8)
No	6 (16.7)	10 (8.6)	9 (5.0)	6 (7.8)	31 (7.6)
I don't know	0	4 (3.4)	9 (5.0)	2 (2.6)	15 (3.7)
N/A (Answered "No" or "I don't know" to Question 26)	38	37	30	66	171

Source: Appendix X, Table 6.1
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 6.1A: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%)	France (N=153) n (%)	Germany (N=160) n (%)	Spain (N=143) n (%)	Overall (N=530) n (%)
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?					
Yes	38 (51.4)	101 (66.0)	63 (39.4)	74 (51.7)	276 (52.1)
No	36 (48.6)	52 (34.0)	97 (60.6)	69 (48.3)	254 (47.9)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]					
Yes	20 (52.6)	67 (66.3)	46 (73.0)	35 (47.3)	168 (60.9)
No	6 (15.8)	15 (14.9)	7 (11.1)	16 (21.6)	44 (15.9)
I don't remember	12 (31.6)	19 (18.8)	10 (15.9)	23 (31.1)	64 (23.2)
N/A (Answered "No" to Question 20)	36	52	97	69	254
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]					
Yes	17 (85.0)	48 (71.6)	33 (71.7)	29 (82.9)	127 (75.6)
No	0	13 (19.4)	7 (15.2)	3 (8.6)	23 (13.7)
I don't remember	3 (15.0)	6 (9.0)	6 (13.0)	3 (8.6)	18 (10.7)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	54	86	114	108	362
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?					
Yes	32 (43.2)	85 (55.6)	92 (57.5)	68 (47.6)	277 (52.3)
No	42 (56.8)	68 (44.4)	68 (42.5)	75 (52.4)	253 (47.7)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]					
Yes	25 (89.3)	42 (91.3)	49 (96.1)	60 (92.3)	176 (92.6)
No	2 (7.1)	3 (6.5)	2 (3.9)	5 (7.7)	12 (6.3)
I don't know	1 (3.6)	1 (2.2)	0	0	2 (1.1)
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	46	107	109	78	340
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]					

Table 6.1A: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Country - Completed Surveys

Question	Country				
	Sweden (N=74) n (%)	**France (N=153) n (%)**	**Germany (N=160) n (%)**	**Spain (N=143) n (%)**	**Overall (N=530) n (%)**
Yes	5 (20.0)	5 (11.9)	4 (8.2)	1 (1.7)	15 (8.5)
No	10 (40.0)	37 (88.1)	40 (81.6)	54 (90.0)	141 (80.1)
I don't know	10 (40.0)	0	5 (10.2)	5 (8.3)	20 (11.4)
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	49	111	111	83	354
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?					
Yes	36 (48.6)	116 (75.8)	137 (85.6)	77 (53.8)	366 (69.1)
No	14 (18.9)	17 (11.1)	12 (7.5)	38 (26.6)	81 (15.3)
I don't know	24 (32.4)	20 (13.1)	11 (6.9)	28 (19.6)	83 (15.7)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]					
Yes	30 (83.3)	102 (87.9)	124 (90.5)	69 (89.6)	325 (88.8)
No	6 (16.7)	10 (8.6)	7 (5.1)	6 (7.8)	29 (7.9)
I don't know	0	4 (3.4)	6 (4.4)	2 (2.6)	12 (3.3)
N/A (Answered "No" or "I don't know" to Question 26)	38	37	23	66	164

Source: Appendix X, Table 6.1A
Note: This table includes only the first 80 dermatologists completing the survey from Germany.
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 6.2: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Presciber (N=486) n (%)	**Potential Prescribers (N=95) n (%)**
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?		
Yes	264 (54.3)	29 (30.5)
No	222 (45.7)	66 (69.5)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]		
Yes	173 (65.5)	10 (34.5)
No	37 (14.0)	8 (27.6)
I don't remember	54 (20.5)	11 (37.9)
N/A (Answered "No" to Question 20)	222	66
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]		
Yes	133 (76.9)	6 (60.0)
No	22 (12.7)	2 (20.0)
I don't remember	18 (10.4)	2 (20.0)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	313	85
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?		
Yes	273 (56.2)	27 (28.4)
No	213 (43.8)	68 (71.6)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]		
Yes	197 (92.5)	0
No	14 (6.6)	0
I don't know	2 (0.9)	0
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	273	95

Table 6.2: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Prescribing Status - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Status	
	Active Presciber (N=486) n (%)	**Potential Prescribers (N=95) n (%)**
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]		
Yes	18 (9.1)	0
No	159 (80.7)	0
I don't know	20 (10.2)	0
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	289	95
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?		
Yes	370 (76.1)	40 (42.1)
No	61 (12.6)	24 (25.3)
I don't know	55 (11.3)	31 (32.6)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]		
Yes	329 (88.9)	35 (87.5)
No	26 (7.0)	5 (12.5)
I don't know	15 (4.1)	0
N/A (Answered "No" or "I don't know" to Question 26)	116	55

Source: Appendix X, Table 6.2
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 6.3: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%)	**Dermatologist (N=333) n (%)**
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?		
Yes	132 (53.2)	161 (48.3)
No	116 (46.8)	172 (51.7)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]		
Yes	87 (65.9)	96 (59.6)
No	16 (12.1)	29 (18.0)
I don't remember	29 (22.0)	36 (22.4)
N/A (Answered "No" to Question 20)	116	172
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]		
Yes	62 (71.3)	77 (80.2)
No	15 (17.2)	9 (9.4)
I don't remember	10 (11.5)	10 (10.4)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	161	237
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?		
Yes	168 (67.7)	132 (39.6)
No	80 (32.3)	201 (60.4)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]		
Yes	67 (94.4)	130 (91.5)
No	3 (4.2)	11 (7.7)
I don't know	1 (1.4)	1 (0.7)
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	177	191

Table 6.3: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Specialty - Completed Surveys Including all Dermatologists from Germany

Question	Specialty	
	Rheumatologist (N=248) n (%)	**Dermatologist (N=333) n (%)**
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]		
Yes	10 (14.9)	8 (6.2)
No	47 (70.1)	112 (86.2)
I don't know	10 (14.9)	10 (7.7)
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	181	203
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?		
Yes	203 (81.9)	207 (62.2)
No	22 (8.9)	63 (18.9)
I don't know	23 (9.3)	63 (18.9)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]		
Yes	188 (92.6)	176 (85.0)
No	12 (5.9)	19 (9.2)
I don't know	3 (1.5)	12 (5.8)
N/A (Answered "No" or "I don't know" to Question 26)	45	126

Source: Appendix X, Table 6.3
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 6.4: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=223) n (%)	**High Prescibers (N=263) n (%)**
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?		
Yes	140 (53.2)	124 (55.6)
No	123 (46.8)	99 (44.4)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]		
Yes	91 (65.0)	82 (66.1)
No	17 (12.1)	20 (16.1)
I don't remember	32 (22.9)	22 (17.7)
N/A (Answered "No" to Question 20)	123	99
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]		
Yes	69 (75.8)	64 (78.0)
No	11 (12.1)	11 (13.4)
I don't remember	11 (12.1)	7 (8.5)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	172	141
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?		
Yes	133 (50.6)	140 (62.8)
No	130 (49.4)	83 (37.2)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]		
Yes	121 (93.1)	76 (91.6)
No	8 (6.2)	6 (7.2)
I don't know	1 (0.8)	1 (1.2)
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	133	140

Table 6.4: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Prescribing Frequency - Completed Surveys Including all Dermatologists from Germany

Question	Prescribing Frequency	
	Low Prescribers (N=223) n (%)	**High Prescibers (N=263) n (%)**
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]		
Yes	12 (9.9)	6 (7.9)
No	92 (76.0)	67 (88.2)
I don't know	17 (14.0)	3 (3.9)
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	142	147
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?		
Yes	189 (71.9)	181 (81.2)
No	37 (14.1)	24 (10.8)
I don't know	37 (14.1)	18 (8.1)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]		
Yes	165 (87.3)	164 (90.6)
No	17 (9.0)	9 (5.0)
I don't know	7 (3.7)	8 (4.4)
N/A (Answered "No" or "I don't know" to Question 26)	74	42

Source: Appendix X, Table 6.4
Note: Low prescribers: <= 5 patients in the last 6 months; High prescribers: => 6 patients in the last 6 months.
Note: This table does not include respondents who answered 'No' to Question 6: 'Have you prescribed Olumiant (baricitinib)?'.
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.

Table 6.5: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%)	Medium (N=460) n (%)	Low (N=11) n (%)
Question 20: Prior to today, were you aware of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?			
Yes	61 (55.5)	227 (49.3)	5 (45.5)
No	49 (44.5)	233 (50.7)	6 (54.5)
Question 21: Did you receive a copy of the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]			
Yes	40 (65.6)	140 (61.7)	3 (60.0)
No	9 (14.8)	36 (15.9)	0
I don't remember	12 (19.7)	51 (22.5)	2 (40.0)
N/A (Answered "No" to Question 20)	49	233	6
Question 22: Have you read the Healthcare Professional Educational Materials for Olumiant (baricitinib)?[a]			
Yes	30 (75.0)	108 (77.1)	1 (33.3)
No	7 (17.5)	16 (11.4)	1 (33.3)
I don't remember	3 (7.5)	16 (11.4)	1 (33.3)
N/A (Answered "No" to Question 20 or "No" or "I don't remember" to Question 21)	70	320	8
Question 23: Prior to today, were you aware of the Patient Alert Card for Olumiant?			
Yes	71 (64.5)	226 (49.1)	3 (27.3)
No	39 (35.5)	234 (50.9)	8 (72.7)
Question 24: Do you or someone in your practice/hospital communicate the important safety information to your patients when prescribing Olumiant (baricitinib) for the first time?[a]			
Yes	31 (83.8)	164 (94.3)	2 (100.0)
No	6 (16.2)	8 (4.6)	0
I don't know	0	2 (1.1)	0
N/A (Answered "No" to Question 6 or "Yes" to Question 23)	73	286	9

Table 6.5: Responses to Questions about Healthcare Professional Educational Material for Olumiant (baricitinib) by Prescriber Experience - Completed Surveys Including all Dermatologists from Germany

Question	Prescriber Experience		
	High (N=110) n (%)	Medium (N=460) n (%)	Low (N=11) n (%)
Question 25: When prescribing Olumiant (baricitinib) for the first time is your patient provided with a Patient Alert Card?[a]			
Yes	5 (16.1)	13 (7.9)	0
No	25 (80.6)	132 (80.5)	2 (100.0)
I don't know	1 (3.2)	19 (11.6)	0
N/A (Answered "No" to Question 6 or "No" or "I don't know" to Question 24)	79	296	9
Question 26: Did you receive a copy of the Direct Healthcare Professional communication [date] to communicate safety regarding all JAK inhibitors?			
Yes	91 (82.7)	313 (68.0)	6 (54.5)
No	12 (10.9)	71 (15.4)	2 (18.2)
I don't know	7 (6.4)	76 (16.5)	3 (27.3)
Question 27: Have you read the Direct Healthcare Professional Communication [date] to communicate safety regarding all JAK inhibitors?[a]			
Yes	79 (86.8)	280 (89.5)	5 (83.3)
No	5 (5.5)	25 (8.0)	1 (16.7)
I don't know	7 (7.7)	8 (2.6)	0
N/A (Answered "No" or "I don't know" to Question 26)	19	147	5

Source: Appendix X, Table 6.5
Note: High experience will be defined as prescriber with >15 years experience and more than 25 RA/Dermatology patients. Low experience will be defined as prescribers with <5 years experience and less than 5 RA/Dermatology patients. All other prescribers will be counted as Medium experience including those with experience missing.
[a] Question was not asked to select respondents due to the skip patterns based on response to previous questions. Therefore, counts and percentages shown are of respondents who were administered this question.