Title Page

Study Title:	Evaluation of Physician and Patient Knowledge of Safety and Safe Use Information for Aflibercept in Europe: An Observational Postauthorisation Study Measurement of effectiveness of risk minimisation measures (Study #16526)
Product:	Eylea (aflibercept)
Indication:	Aflibercept has been approved by the European Medicines Agency (EMA) in adults for treatment of the following indications: • Neovascular (wet) age-related macular degeneration (wAMD) • Visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO) • Visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO) • Visual impairment due to diabetic macular oedema (DME) • Visual impairment due to myopic choroidal neovascularisation (myopic CNV)[1]
Sponsor's Name and Address:	**Bayer AG**, 51368 Leverkusen, Germany
Study Number:	16526
Development phase:	Post-authorization
Study Date:	First patient first visit: 07 December 2015 Last patient last visit: 29 September 2016
Investigator(s):	Multi-center, a list of investigators is available on request
Date:	05 June 2017
Signatures:	*I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.*

[1] Aflibercept was approved for the treatment of myopic CNV after the study protocol was final.

[redacted]		Date		[redacted]		Date
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[redacted]		Date		[redacted]		Date

Confidentiality statement:

This document contains information that is privileged or confidential and may not be disclosed for any purposes without the prior written consent of a Bayer group company.

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Confidentiality statement:

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see below for signature [redacted]	Date	[redacted]	6 June 2017 Date
		[redacted]	6 June 2017

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PASS information

Title	Evaluation of Physician and Patient Knowledge of Safety and Safe Use Information for Aflibercept in Europe: An Observational Postauthorisation Study Measurement of effectiveness of risk minimisation measures (Study #16526)
Version identifier of the final study report	Version 1.0
Date of last version of the final study report	05 June 2017
EU PAS register number	EUPAS9991
Active substance	INN: Aflibercept; ATC code: S01LA05
Product	Eylea (aflibercept)
Product reference	EU/1/12/797/001 and EU/1/12/797/002
Procedure number	EMA/H/C/0002392
Marketing authorisation holder(s)	Bayer AG
Joint PASS	No
Research question and objectives	Postapproval commitment to initial AMD MAA PASS (MEA004) for a postauthorisation safety study to evaluate physician and patient knowledge of information on safety and safe use for Eylea in Europe. The primary objective of this study is to measure physician and patient knowledge and understanding of key information contained in the Eylea educational materials: the prescriber guide and video, and the patient booklet "Your Guide to EYLEA," patient information leaflet, and audio CD. Specifically, the following objectives were addressed: ▪ Investigate whether physicians and their patients have received the educational materials ▪ Assess physicians' knowledge and understanding of key safety information contained in the prescriber guide and the intravitreal injection procedure video and assess how physicians used the materials in their daily practice ▪ Assess patients' knowledge and understanding of the key safety information contained in the patient booklet "Your Guide to EYLEA," patient information leaflet, and audio CD and determine if the patients used this information.
Country(-ies) of study	The United Kingdom, Germany, France, Spain, and Italy
Author	[redacted]

Marketing authorisation holder(s)

Marketing authorisation holder(s)	Bayer AG D-13342 Berlin Germany
MAH contact person	

Study Design Description		
Study Sponsor:	Bayer AG	
Study Number:	16526	NCT02615496
Study Phase:	Post-authorization	
Official Study Title:	Evaluation of Physician and Patient Knowledge of Safety and Safe Use Information for Aflibercept in Europe: An Observational Postauthorisation Study Measurement of effectiveness of risk minimisation measures	
Therapeutic Area:	Ophthalmology	
Product		
Name of observed Product:	Aflibercept (Eylea, BAY 86-5321)	
Name of Active Ingredient:	Aflibercept	
Dose and Mode of Administration:	Not applicable	
Reference Therapy		
Reference Therapy:	Not applicable	
Dose and Mode of Administration:	Not applicable	
Duration of Treatment:	Not applicable	
Studied period: *Note: in retrospective studies, start/end of study is defined differently.*	Date of first patient first visit:	07 December 2015
	Date of last patient last visit:	29 September 2016
Study Center(s):	46 sites in 5 countries: 6 sites in France, 10 sites in Germany, 10 sites in Italy, 9 sites in Spain, and 11 sites in the UK	
Methodology:	The study was an observational, cross-sectional study among physicians and patients with recent aflibercept experience. Eligible physicians and patients were invited to complete a brief questionnaire regarding their knowledge of key safety in the aflibercept educational materials.	
Indication/ Main Inclusion Criteria:	Physicians were eligible to participate if they had prescribed or administered aflibercept in the past 6 months. Patients were eligible if they had been administered an aflibercept injection within the past 6 months.	

Study Objectives:	Primary: ▪ Investigate whether physicians and their patients have received the educational materials ▪ Assess physicians' knowledge and understanding of key safety information contained in the prescriber guide and the intravitreal injection procedure video and assess how physicians used the materials in their daily practice ▪ Assess patients' knowledge and understanding of the key safety information contained in the patient booklet "Your Guide to EYLEA," patient information leaflet, and audio CD and determine if the patients used this information.
Evaluation Criteria:	Primary objective(s): Results from this study (e.g., % responding correctly) were reviewed qualitatively to identify patterns suggesting the educational activities have been successful (e.g., consistently high percentages of correct responses across all questions), not successful (e.g., consistently low percentages of correct responses), or partially successful (e.g., high percentages for most responses and low for selected responses).
Statistical Methods:	Data analyses were descriptive in nature and focused primarily on summarising the questionnaire responses.
Number of Participants:	The target sample size was 300 to 500 physicians overall, and the study achieved 428 completed physician questionnaires (69 in France, 59 in Germany, 99 in Italy, 102 in Spain, and 99 in the UK). The target sample size was 750 patients overall, and the study achieved 773 completed patient questionnaires (114 in France, 158 in Germany, 168 in Italy, 169 in Spain, and 164 in the UK).
Early Termination:	No
Substantial Protocol Changes:	None

Study Results

Results Summary — Patient Disposition and Baseline

A total of 8,424 physicians were invited to participate and 798 completed the screener. Of these, 14 did not consent, 339 were ineligible, and 17 did not meet the definition for a completed questionnaire.

Of the 874 patients approached to participate, 23 were ineligible. Of the 851 patients who were eligible, 75 declined, 2 did not consent, and 1 did not meet the definition for a completed questionnaire.

Results Summary — Primary [and Secondary] Objectives

In general, physicians' knowledge of questions related to aflibercept storage and preparation and injection procedures was high. Physician knowledge on dosing requirements was higher for wAMD and lower for newer or less commonly prescribed indications. Some physicians responded that monitoring is required during the first 12 months for the treatment of wAMD and the treatment of DME even though there is no requirement for monitoring between injections during the first 12 months. Most physicians knew the recommended dose for aflibercept, and knowledge on questions related to excess volume of aflibercept varied. Overall, physicians' knowledge of actions to prepare patients for treatment with aflibercept was high, and most physicians knew the contraindications for aflibercept use. Knowledge was also high for recognising signs and symptoms of possible side effects.

Most physicians reported that they received the SmPC and the prescriber guide. Approximately half of physicians reported that they received the intravitreal injection procedure video and the patient booklet. Likewise, half of physicians reported providing the patient booklet to most or all of their patients.

Patients' knowledge of the health conditions to discuss with a doctor prior to injection was high for 8 out of 9 individual items. Approximately half of patients correctly responded to the question related to pregnancy and breastfeeding, likely because this condition is less salient in the aflibercept patient population given the patients' ages (99% of the patients in the study were 46 years or older). Patient knowledge about possible side effects with aflibercept varied by item. Most patients knew that they should speak to their ophthalmologist (or someone in his or her office) immediately if they think they might be having a side effect from their aflibercept injection.

The levels of reported receipt of the aflibercept patient booklet and the audio CD were relatively low, and there was considerable variation across countries.

Results Summary — Safety

Not applicable

[Results Summary — Other]

Not applicable

Conclusion(s)

Physicians' knowledge of most important topics was high (e.g., side effects). Knowledge was lower for topics that are less frequently encountered (e.g., use in women of childbearing potential) and for more complex aspects of safe use (e.g., dosing and monitoring) for which we assume that physicians would consult the label and/or prescriber guide rather than relying on recall. The reported receipt of the SmPC and prescriber guide was high, and the high level of knowledge among treating physicians also suggests that the key safety information is available to the treating physicians. Levels of patient knowledge were as expected – with highest knowledge on less complex concepts (e.g., health conditions to discuss with the physician and easily identified side effects) and lower knowledge on more complex concepts and issues less salient to the patient population (e.g., more complex side effects and issues pertaining to women of childbearing potential).

Publication(s):	Manuscript in progress
Date Created or Date Last Updated:	15 Nov 2017

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1 Abstract

Title

Evaluation of Physician and Patient Knowledge of Safety and Safe Use Information for Aflibercept in Europe: An Observational Postauthorisation Study

05 June 2017

Laurie Zografos, BS; RTI Health Solutions, Research Triangle Park, NC

Elizabeth Andrews, MPH, PhD; RTI Health Solutions, Research Triangle Park, NC

Keywords

Eylea (aflibercept); postauthorisation safety study; evaluation of risk minimisation measures; physician survey; patient survey

Rationale and background

As part of the risk management plan for aflibercept, Bayer developed materials to educate both physicians and patients on the key safety information and safe use for aflibercept and distributed these materials to increase awareness and understanding about risks associated with aflibercept. The current study was conducted to evaluate the understanding and use of these materials.

Research question and objectives

The primary objectives were to measure whether physicians and patients received and used the educational materials and to evaluate their awareness and understanding of the key safety messages.

Study design

The study was an observational, cross-sectional study among physicians and patients with recent aflibercept experience. Eligible physicians and patients were invited to complete a brief questionnaire regarding their knowledge of key safety in the aflibercept educational materials.

Setting

The UK, Germany, France, Spain, and Italy

Subjects and study size, including dropouts

Physicians were eligible to participate if they had prescribed or administered aflibercept in the past 6 months for one of the indications of interest. A total of 8,424 physicians were invited to participate and 798 completed the screener. Of these, 14 did not consent, 339 were ineligible, and 17 did not meet the definition for a completed questionnaire. The target sample size was 300 to 500 physicians overall, and the study achieved 428 completed physician questionnaires, for a response rate of 5.1%.

Patients were eligible if they had been administered an aflibercept injection within the last 6 months for one of the indications of interest. Of the 874 patients approached to participate, 23 were ineligible. Of the 851 patients who were eligible, 75 declined, 2 did not consent, and 1 did not meet the definition for a completed questionnaire. The target sample size was 750 patients overall, and the study achieved 773 completed patients questionnaires, for a response rate of 91%.

Variables and data sources

Data were obtained through questionnaire responses.

Results

In general, physicians' knowledge of questions related to aflibercept storage and preparation and injection procedures was high. Physician knowledge on dosing requirements was higher for wAMD and lower for newer or less commonly prescribed indications. Some physicians responded that monitoring is required during the first 12 months for the treatment of wAMD and the treatment of DME even though there is no requirement for monitoring between injections during the first 12 months. Most physicians knew the recommended dose for aflibercept, and knowledge on questions related to excess volume of aflibercept varied. Overall, physicians' knowledge of actions to prepare patients for treatment with aflibercept was high, and most physicians knew the contraindications for aflibercept use. Knowledge was also high for recognising signs and symptoms of possible side effects.

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Patients' knowledge of the health conditions to discuss with a doctor prior to injection was high for 8 out of 9 individual items. Approximately half of patients correctly responded to the question related to pregnancy and breastfeeding, likely because this condition is less salient in the aflibercept patient population given the patients' ages (99% of the patients in the study were 46 years or older). Patient knowledge about possible side effects with aflibercept varied by item. Most patients knew that they should speak to their ophthalmologist (or someone in his or her office) immediately if they think they might be having a side effect from their aflibercept injection.

The levels of reported receipt of the aflibercept patient booklet and the audio CD were relatively low, and there was considerable variation across countries.

Discussion

Physicians' knowledge of most important topics was high (e.g., side effects). Knowledge was lower for topics that are less frequently encountered (e.g., use in women of childbearing potential) and for more complex aspects of safe use (e.g., dosing and monitoring) for which we assume that physicians would consult the label and/or prescriber guide rather than relying on recall. The reported receipt of the SmPC and prescriber guide was high, and the high level of knowledge among treating physicians also suggests that the key safety information is available to the treating physicians. Levels of patient knowledge were as expected – with highest knowledge on less complex concepts (e.g., health conditions to discuss with the physician and easily identified side effects) and lower knowledge on more complex concepts and issues less salient to the patient population (e.g., more complex side effects and issues pertaining to women of childbearing potential).

Marketing Authorisation Holder(s)

Bayer AG

Names and affiliations of principal investigators

Elizabeth Andrews, MPH, PhD; RTI Health Solutions, Research Triangle Park, NC; Laurie Zografos, BS; RTI Health Solutions, Research Triangle Park, NC

2 List of Abbreviations

AE	adverse event
ATC	Anatomical Therapeutic Chemical Classification System
BRVO	branch retinal vein occlusion
CI	confidence interval
CRVO	central retinal vein occlusion
DME	diabetic macular oedema
EMA	European Medicines Agency
ENCePP	European Network of Centres of Pharmacoepidemiology and Pharmacovigilance
PASS	postauthorisation safety studies
RTI HS	RTI Health Solutions
SmPC	summary of product characteristics
US	United States
VEGF	vascular endothelial growth factor
wAMD	wet age-related macular degeneration

3 Investigators

This section provides information for the study principal investigator as well as the country-level investigators. A full list of site-level investigators who participated in the patient assessment is available in a stand-alone document and can be provided upon request.

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[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

4 Other Responsible Parties

Bayer AG is the marketing authorisation holder of Eylea (aflibercept) and the sponsor of the study. RTI Health Solutions (RTI-HS), an independent nonprofit research organisation, is responsible for the design, conduct, analysis, and reporting of the study. Bayer collaborated with RTI-HS on the study design and is also responsible for fulfilling any obligations for reporting results to regulatory agencies. Kantar Health, a global research operations partner, was responsible for cognitive pretesting of the questionnaires, ethics committee submissions, physician recruitment, monitoring sites for patient recruitment, and data collection.

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5 Milestones

Milestone	Actual Date	Comments
Registration in the EU PAS Register	21 June 2016	
Start of data collection	07 December 2015	
End of data collection	24 October 2016	
Lead ethics committee approvals		
France	10 June 2015	
Germany	05 October 2015	
Italy	09 November 2015	
Spain	27 May 2015	
UK	29 May 2015	
Data collection for physician assessment		
France	20 April 2016 to 25 July 2016	
Germany	20 April 2016 to 24 October 2016	
Italy	20 April 2016 to 02 June 2016	
Spain	20 April 2016 to 31 May 2016	
UK	20 April 2016 to 07 October 2016	

Milestone	Actual Date	Comments
Data collection for patient assessment		
France	28 January 2016 to 25 September 2016	
Germany	07 December 2015 to 26 August 2016	
Italy	11 March-2016 to 28 September 2016	
Spain	16 March 2016 to 29 September 2016	
UK	23 December 2015 to 25 August 2016	
Final report of study results	5 June 2017	

6 Rationale and Background

Eylea (aflibercept) is a compound administered as an intravitreal injection. Aflibercept is a fusion protein specifically designed to bind all forms of vascular endothelial growth factor A (VEGF-A) and placental growth factor, two proteins involved in the abnormal growth of new blood vessels (Eylea SmPC, 2016).

Aflibercept has been approved by the European Medicines Agency (EMA) in adults for the treatment of neovascular (wet) age-related macular degeneration (wAMD), visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO), visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO), visual impairment due to diabetic macular oedema (DME), and visual impairment due to myopic choroidal neovascularisation (myopic CNV)[2].

Intravitreal injections, including anti-VEGF therapies, have been associated with some uncommon complications, such as endophthalmitis, transient increases in intraocular pressure, traumatic cataract, and retinal and vitreous detachment. Publications cite the frequency of those complications associated with the use of intravitreal injections ranges from less than 1% to 2%. Less serious and more common complications include conjunctival haemorrhage, vitreous floaters, and eye pain (Csaky and Do, 2009; Jeganathan and Verma, 2009). Some reports based on exposure to the anti-VEGF therapies ranibizumab (Lucentis) and bevacizumab (Avastin) have noted the potential of such therapies to increase the risk of experiencing coronary heart disease, cerebrovascular disease, or both (Csaky and Do, 2009; Micieli et al., 2010), suggesting a possible class effect.

As part of the EU risk management plan for aflibercept, Bayer developed materials to educate both physicians and patients on the key safety information and safe use for aflibercept. The EU educational materials are intended to raise physicians' awareness and minimise the occurrence and consequences of the important identified risks of endophthalmitis, intraocular inflammation, transient intraocular pressure increase, epithelium tears, traumatic cataract, embryo and fetotoxicity, medication error, misuse, and off-label use. The key content of the educational materials for physicians includes the importance of using the correct sterile injection technique and monitoring and managing potential injection-related adverse events (AEs). Key content for patients includes steps for preparing for treatment, monitoring for AEs, and steps to take if they identify AEs.

Bayer collaborated with RTI-HS to design and conduct this study to evaluate the effectiveness of the aflibercept educational materials and to gain a better understanding of physician and patient knowledge of the key safety information and safe use for aflibercept.

7 Research Question and Objectives

The primary objective of this study is to measure physician knowledge and understanding of the key information in the prescriber guide and intravitreal injection procedure video and patient knowledge and understanding of the key information contained in the patient booklet "Your Guide to EYLEA," patient information leaflet, and audio CD.

Specifically, the following objectives were addressed:

[2] The study eligibility criteria were broad enough to include physicians and patients who had recent experience with any of the aflibercept indications at the time of data collection; however, the questionnaire only included questions specific to the aflibercept indications that were approved at the time of questionnaire development.

- Investigate whether physicians and their patients have received the educational materials
- Assess physicians' knowledge and understanding of key safety information contained in the prescriber guide and the intravitreal injection procedure video and assess how physicians use the materials in their daily practice
- Assess patients' knowledge and understanding of the key safety information contained in the patient booklet "Your Guide to EYLEA," patient information leaflet, and audio CD and determine if the patients used this information

As part of good research practices, the protocol and ENCePP checklist were registered in the EU PAS Register (ENCePP, 2016a) prior to the start of data collection. The study was designed and implemented in line with the International Society for Pharmacoepidemiology *Guidelines for Good Pharmacoepidemiology Practices* (ISPE, 2015); European Medicines Agency *Guidelines on Good Pharmacovigilance Practices, Module VIII – Postauthorization Safety Studies* (EMA, 2016); and ENCePP *Guide on Methodological Standards in Pharmacoepidemiology* (ENCePP, 2016b). The contract between RTI-HS and Bayer includes independent publication rights.

The study received exemption from review by the RTI International Institutional Review Board on 23 January 2015.

8 Amendments and Updates

None

9 Research Methods

9.1 Study Design

The study was an observational, cross-sectional study of knowledge, understanding, and self-reported behaviour among a sample of physicians and patients with recent aflibercept experience in a total of five European countries. Eligible physicians and patients were invited to complete a brief questionnaire regarding their knowledge of key safety messages as outlined in the aflibercept educational materials. A cross-sectional survey approach was selected for this study because the main information on knowledge and understanding of the educational material could be obtained only through direct interaction with physicians and patients.

9.1.1 Physician Assessment

The physician assessment was initiated in each country after a period of time following product launch deemed sufficient to allow prescribers to have received the prescriber education packets and use the information in their practice. Physicians were primarily recruited by selecting a random sample of physicians from an online physician panel made up of convenience samples of physicians derived from multiple sources (e.g., hospital books, medical directories, peer referrals) with the aim of obtaining a sample generally representative of physicians who have prescribed aflibercept in the selected countries and according to the approved indications. In addition, to supplement the panel in Germany, physicians were identified from a list provided by Bayer. Invitations were sent via e-mail and made by phone to the selected sample of physicians, inviting them to participate and providing a link to a web-based questionnaire. Interested physicians logged in to the study website by entering a unique identification number and password. They then completed an informed consent and a screening question to confirm that they were licensed and practicing ophthalmologist and had prescribed and/or administered at least one aflibercept injection within the past 6 months. Physicians who completed the

consent and passed the screening question could continue and complete the self-administered questionnaire (Annex 3).

The web-based format for completion of the consent form and self-administered questionnaire was chosen because of the efficiency and utility of the mode (e.g., question branching logic and ability to stop participants from going back to previous questions to change answers). Most physicians have convenient access to complete a web-based questionnaire, so the use of this technology is not believed to have introduced a respondent bias.

At the time of questionnaire development, the educational materials included information on two injectable forms of aflibercept, a vial and a prefilled syringe. The questionnaire therefore included items about both injectable forms. However, the prefilled syringe was never marketed and was not available to physicians, making the questions about the prefilled syringe not applicable. As such, the findings for questions related to the prefilled syringe are not included in this report. However, in their responses some physicians erroneously indicated that they had used the prefilled syringe but had not used the vial. This did impact the number of respondents to five of the questions on the survey because a skip pattern was enforced so the questions were only asked of those who indicated they used the vial form. Counts of patients who skipped the question due to the skip pattern are included in the tables.

9.1.2 Patient Assessment

A total of 46 ophthalmology medical practices (sites) were selected from lists of physicians identified by Bayer that were known to prescribe aflibercept. Geographic location was evaluated to ensure a diverse representation of sites that reflected prescribing practices in each country. Sites were contacted to determine interest in the study, to confirm eligibility, and to assess the feasibility of implementing data collection at each site. The sites selected for participation in the patient assessment were excluded from the physician assessment described above; however, participating physicians from the sites included in the patient assessment were asked to complete the physician questionnaire to allow exploratory evaluation of the possible impact of the study on physician knowledge and to evaluate patient responses by level of knowledge of their physician. Questionnaire responses from the two different groups of physicians were analysed separately.

The patient assessment was initiated after the new educational materials had been disseminated. Patients were invited to participate only after they had received at least one aflibercept injection within the last 6 months for any indication such that they had had an opportunity to receive the educational materials and their recall of receiving, reading, and carrying the materials could be evaluated. Eligible patients who were present for a scheduled visit were invited to participate by their physicians. To minimise the possibility of a study intervention effect, sites were trained not to discuss the study with patients in advance of their visit so as not to allow patients to prepare for the survey beforehand. Those patients who consented completed an interviewer-administered questionnaire (Annex 4). Sites were asked not to deviate from their customary patient counselling practices and were asked to administer the questionnaire to patients during the visit prior to any patient counselling. In order to ensure representation across all aflibercept indications, each site was asked to recruit at least one patient in each indication if possible.

The interview format for completion of the questionnaire was chosen based on the results of the cognitive interviews, which indicated that the target patient population may have age-related cognitive difficulties (e.g., slow thinking, poor concentration, and memory issues) in addition to visual impairment and suggested that some patients may need assistance with completing the questionnaire. Site personnel were trained to ensure a

thorough understanding of the importance of and processes for conducting an objective interview to mitigate potential biases and an "intervention effect."

Each participating site kept a simple log, collecting de-identified information (i.e., sex, age range, indication for which aflibercept was prescribed, approximate date of first aflibercept injection, and number of injections in the past 12 months) on all patients eligible to participate to evaluate any differences between participants and non-participants that should be considered in the analysis. Patients who were approached by the study coordinator and then refused to participate were asked their reason for refusal.

To encourage diversity among the patients participating, enrolment was targeted at 10 patients per site. Towards the end of the data collection period, some sites were allowed to enrol additional patients to compensate for sites unable to recruit the targeted sample. However, enrolment was capped at 30 patients per site to prevent any site from providing more than 5% of the overall study population.

9.2 Setting

This study was conducted in France, Germany, Italy, Spain, and the UK. The five countries included were chosen to provide some diversity in practice patterns and patient treatment indication, and to observe differences in physician and patient knowledge in these settings. In addition, prescribing levels in these countries were such that there was a sufficient number of eligible physicians and patients with aflibercept experience to participate in the study.

Data collection for the physician assessment ran from 20 April 2016 to 24 October 2016, and data collection for the patient assessment ran from 7 December 2015 to 29 September 2016.

9.3 Subjects

9.3.1 Physician Assessment

9.3.1.1 Physician Eligibility

This study was conducted with physicians (ophthalmologists) who prescribe and administer aflibercept in the target countries.

To be eligible for the study, physicians met all of the following eligibility criteria:

- Licensed and practising ophthalmologist
- Prescribed and administered aflibercept to at least one patient in the past 6 months

9.3.2 Patient Assessment

9.3.2.1 Site Eligibility

To participate in the study, sites met the following criteria:

- Saw a sufficient number of eligible patients to recruit at least 10 to complete the questionnaire
- Had a staff member available to administer the questionnaire to patients
- Were able to provide a semiprivate space for patient recruitment, the consent process, and completion of the interviewer-administered questionnaire
- Had a staff member available to coordinate research activities

9.3.2.2 Patient Eligibility

To avoid selecting patients who just have received the educational material at the same visit, only those who had already received at least one aflibercept injection within the last 6 months and were returning for a subsequent visit were recruited.

To be eligible for the study, the patients met all of the following criteria:

- Patient had been administered aflibercept at least once within the last 6 months for any indication and was returning for a subsequent visit
- Patient was aged 18 years or older
- Patient was able to understand and sign the consent form and complete the questionnaire
- Patient could understand the native language of the country in which the study was being conducted
- Patient had not participated in a clinical trial for the treatment of an aflibercept indication (e.g., wAMD, CRVO, or DME) in the past 12 months

9.4 Variables

9.4.1 Physician Questionnaire

The physician questionnaire was based on the educational materials available at the time the questionnaire was developed. It contained closed-ended questions (e.g., multiple choice, true/false), with no free-text response fields, eliciting responses measuring physician knowledge and understanding of the key information in the Eylea Prescriber Guide and video. The physician questionnaire included items in the following content areas:

- Storage and preparation of aflibercept
- Aflibercept dosing and monitoring recommendations (specific to indications approved at the time of questionnaire development)
- Preparing the patient for treatment with aflibercept
- Aflibercept contraindications
- Sterile techniques to minimise risk of infection, including periocular and ocular disinfection
- Use of povidone iodine or equivalent
- Techniques for the intravitreal injection
- Key signs and symptoms of intravitreal injection–related AEs (i.e., endophthalmitis, cataract, transient intraocular pressure increase, vitreous detachment, and conjunctival and retinal haemorrhage) and medication error/overdose

In addition to these concepts, the physician questionnaire included items to characterise the physicians and their practices (e.g., years in practice, patient volume, indications treated with aflibercept) and to investigate physician receipt and use of the prescriber educational materials.

9.4.2 Patient Questionnaire

The patient questionnaire was based on the educational materials available at the time the questionnaire was developed. It contained primarily closed-ended questions (e.g., multiple choice, true/false) eliciting responses measuring patient knowledge and understanding of the key information contained in the aflibercept patient

booklet "Your Guide to EYLEA," patient information leaflet, and audio CD. The patient questionnaires included items in the following content areas:

- Conditions that patients should tell their doctor about before receiving aflibercept
- Key signs and symptoms of AEs (i.e., endophthalmitis, cataract, temporary increase of pressure inside the eye, vitreous detachment, vitreous floaters, and conjunctival haemorrhage)
- What patients should do if they develop a symptom or a suspected side effect

In addition to these concepts, the patient questionnaire included items to investigate patient receipt and use of the patient booklet "Your Guide to EYLEA," patient information leaflet, and audio CD, as well as patient characteristics.

9.5 Data Sources and Measurement

The source of information for the study was self-reported data collected from physicians and patients using standard questionnaires with primarily closed-ended response choices.

Questionnaires for physicians and patients were developed using best practices for instrument development. The questions were tailored to the study aims and the information provided in the aflibercept educational materials. Additional questions were included to obtain information needed to describe the study populations and to assess potential differences across subgroups.

To thoroughly evaluate the physician and patient questionnaires before fielding the study, the questionnaires were tested through cognitive interviews with physicians and patients in France, Germany, Italy, Spain, and the UK. The pretest interviews helped to identify problems with questionnaire items, wording, response choices, etc., and were used to confirm the appropriate mode of questionnaire administration for patients. Likewise, the cognitive testing helped to identify cultural or translational issues with the draft questionnaires so that they could be modified to meet the individual needs of each country while maintaining comparability across the study.

Nine interviews with physicians and 11 interviews with patients were first conducted in the UK to identify issues and optimise wording in English. After the UK interviews, the questionnaires were revised and translated into French, German, Italian, and Spanish. Four interviews with physicians and four interviews with patients then were conducted in each of the four remaining countries (32 total interviews) to confirm wording and facilitate cultural adaptation to each country. Changes to both questionnaires were made based on the results of the cognitive testing.

9.6 Bias

In any observational study, researchers must address the potential for biases, particularly if there is a possibility that the respondents are not representative of the target population. Likewise, the potential for intervention effects and/or response error may present additional sources of bias. Efforts were made to both minimise and identify potential sources of bias in this study as described below.

9.6.1 Cognitive Pretesting

As noted above, the physician and patient questionnaires were cognitively pretested prior to data collection in order to identify any problems with the questionnaire items, wording, and response choices, to confirm appropriate mode of administration, and to ensure consistency across cultures and languages. The questionnaires were modified based on feedback from the cognitive interviews with physicians and patients.

This process helped to ensure that the questions measured the appropriate concepts consistently and accurately across all countries, and thus was intended to minimise bias in responses.

9.6.2 Sample Selection

To minimise sampling bias in the physician assessment, physicians were randomly selected and invited to participate. Although a comparison of participating physician characteristics to non-participating physicians was not possible within the panel recruitment framework, the diversity of physician characteristics and experience with aflibercept in the final sample gave some assurance that the target population was well represented.

For the patient assessment, sites' geographic location was evaluated to ensure a diverse representation of sites that reflected prescribing practices in each country. Each site kept a simple log of information on the number of patients approached about the study, the number of patients confirmed eligible, and the number of patients who refused. Information on sex, age range, indication for which aflibercept was prescribed, approximate date of first aflibercept injection, and number of aflibercept injections in the past 12 months was collected on all eligible patients. Patients who were invited to participate and then refused were asked their reason for refusal.

However, despite efforts to ensure representative samples for both the physician and patient assessments, participants may have differed from non-participants on key characteristics measured in the questionnaire (e.g., education, knowledge, reading the educational materials). For patients, the recruiting sites may have differed in their treated population and/or education practices from sites not selected to participate in the study. The direction and magnitude of such potential bias is not known.

9.6.3 Data Collection Methods

The physician assessment was administered as an online questionnaire. Physicians were not able to go back to previous questions, thus prohibiting them from changing their answers based on subsequent questions.

For the patient assessment, participants were recruited by their treating physician and completed the interviewer-administered questionnaire during a normal visit to the site. As such, there was potential for these patients to receive additional education about the key safety messages for aflibercept beyond what would typically be provided and thus potentially resulted in an overestimate of knowledge among patients. To minimise the potential for this intervention, sites were trained not to provide any additional education to patients nor discuss specific details of the study with patients before their visit, so that patients could not prepare beforehand. However, it is unknown whether this practice occurred, and, if so, what the impact on the study results would be. In addition, site personnel were trained on the importance of and processes for conducting an objective interview. The questionnaire was administered without the aid of a patient booklet for referral, thus relying on patients' recall of the key messages for completion.

9.7 Study Size

For the physician assessment, the target sample size was 60 to 100 per country, for a total of 300 to 500 overall. Ultimately, the study enrolled 428 physicians, ranging from 59 in Germany to 102 in Spain. With a sample size of 428 physician responses for a given question, the maximum width of an exact 95% confidence interval (CI) around the percentage who responded correctly was 9.7% for the physician assessment.

For the patient assessment, the target sample size was 150 per country, for a total of up to 750 overall. Ultimately, the study enrolled 773 patients, ranging from 114 in France to 169 in Spain. With a sample size of 114 patient responses for a given question, the maximum width of an exact 95% CI around the percentage who

responded correctly was 19%; with a sample size of 169, the maximum width was 15.6%; with a sample size of 773, the maximum width was 7.2%.

9.8 Data Transformation

The following summary variables were derived to facilitate evaluation and interpretation of the study results. Most variables used in the analysis did not require any transformation.

9.8.1 Physician Assessment

Derived variables were created for each of the six knowledge questions (i.e. questions 10, 11, 12, 15, 20, and 21) that asked the respondent to "select all that apply" and had more than one correct response; these variables indicated the number of correct responses selected. Derived variables were also created for four composite knowledge questions (i.e. questions 1, 3, 4, and 5) that asked respondents multiple yes/no items; these variables indicated the number of correct items within each question.

9.8.2 Patient Assessment

Derived variables were created for each of the two composite knowledge questions (i.e. questions 1 and 2) that asked respondents multiple yes/no items; these variables indicated the number of correct items selected within each question.

9.9 Statistical Methods

All analyses were performed using SAS 9.4 statistical software (SAS Institute, Inc., Cary, North Carolina). No formal hypothesis testing was conducted.

9.9.1 Main Summary Measures

Data analyses were descriptive in nature and focused primarily on summarising the questionnaire responses. Summary tables consisting of frequencies with percentages were created for all closed-ended questionnaire responses. Open-ended text responses were reported in a listing. Response distribution percentages for a question were based on the total number of respondents who had an opportunity to answer the question. This total excluded those who were asked to skip due to an answer given in a prior question (skip pattern). The sum of respondents who were asked to skip was listed in a row labelled "Not applicable skip pattern" under the question with no percentage calculated for that row. The counts of respondents who had an opportunity but did not answer were included in the row labelled "No answer" with a calculated percentage.

9.9.2 Main Statistical Methods

9.9.2.1 Analysis of Physician Questionnaire

For the physician assessment, the analysis population consisted of respondents who were eligible for the study, provided informed consent, and completed at least one knowledge question in full (question 5 through question 22).

Questionnaire items were divided into the following categories: (1) physician experience with aflibercept, (2) physician characteristics, (3) physician knowledge, (4) physician receipt and use of aflibercept educational materials, (5) physician ratings of aflibercept education materials, and (6) physician use of patient booklet. Separate analysis tables for each category were generated to display the response distributions of all questions, by country and overall.

In addition, the knowledge questions were stratified as follows to explore the association between each variable and physician knowledge levels:

- All knowledge questions were stratified by the physicians' experience with the Eylea Prescriber Guide (based on response to question 24)
- Question 1 (storage and preparation for aflibercept) was stratified by who has primary responsibility for preparation of an aflibercept injection (based on response to screener question 4)

The main physician results tables only include those physicians who participated in the physician assessment (also referred to as *non-recruiting physicians*) and do not include physicians who participated in the patient recruitment (also referred to as *recruiting physicians*). The recruiting physicians completed the same questionnaire as the non-recruiting physicians and the same main set of analysis tables were created to summarise the responses obtained from the recruiting physicians. Recruiting physician results were stratified by country but not by any other variables.

Exact 95% CIs around the percentage of physicians that answered each knowledge question correctly were generated using the Clopper-Pearson method. These CIs were calculated for the overall and by-country result tables but not for the stratified tables.

9.9.2.2 Analysis of Patient Questionnaire

For the patient assessment, the analysis population consisted of respondents who were eligible for the study, and completed at least one knowledge question in full (question 1 through question 3).

Questionnaire items were divided into the following categories: (1) patient characteristics, (2) patient knowledge, (3) patient preinjection instructions and receipt of aflibercept educational materials, and (4) patient use of aflibercept education materials. Separate analyses tables for each category were generated to display the response distributions of all questions, by country and overall.

In addition, all knowledge questions have been stratified by the following variables to explore the association between each variable and patient knowledge levels:

- Patients' experience with the Eylea Patient Booklet (based on response to questions 5 and 7)
- Help patient received from anyone other than their doctor or nurse (based on response to question 12)

Exact 95% CIs for the knowledge questions, by country and overall, were calculated using the Clopper-Pearson method. This method assumed independence between patients, which was determined to be appropriate despite the design of sampling multiple patients per site because the observed intra-class correlation among the patients within the sites was relatively low, ranging between 0.05 to 0.15 for almost all of the knowledge questions.

9.9.3 Missing Values

No imputation of missing values was performed.

9.9.4 Sensitivity Analyses

None

9.9.5 Amendments to the Statistical Analysis Plan

None

9.9.6 Quality Control

This project was conducted in accordance with internal standard operating procedures of participating institutions. The RTI-HS Office of Quality Assurance, an independent unit that reports to the Vice President of RTI-HS, oversaw quality assurance for this study.

Standard operating procedures (SOPs) were used to guide the conduct of the study. These procedures included rules for secure and confidential data storage, methods to maintain and archive project documents, quality-control procedures for programming, standards for writing analysis plans, and requirements for senior scientific review.

In accordance with relevant SOPs, the initial programmer reviewed all programme log files for errors and warning messages and retained electronic copies of all final log files in the project folder. The programmer accounted for the number of observations reported at each executed data step and noted in the programme code when the number of observations increased or decreased. Listings or output used to verify results were output and preserved in the quality-control folder or in the programme folder. A second programmer independently wrote programme code and confirmed the findings of the initial programmer. A quality-control checklist has been maintained for the project; and a hard copy was printed, signed, and retained in the project folder.

All key study documents, such as the analysis plan, questionnaires, and study reports, underwent quality-control review, senior scientific review, and editorial review.

10 Results

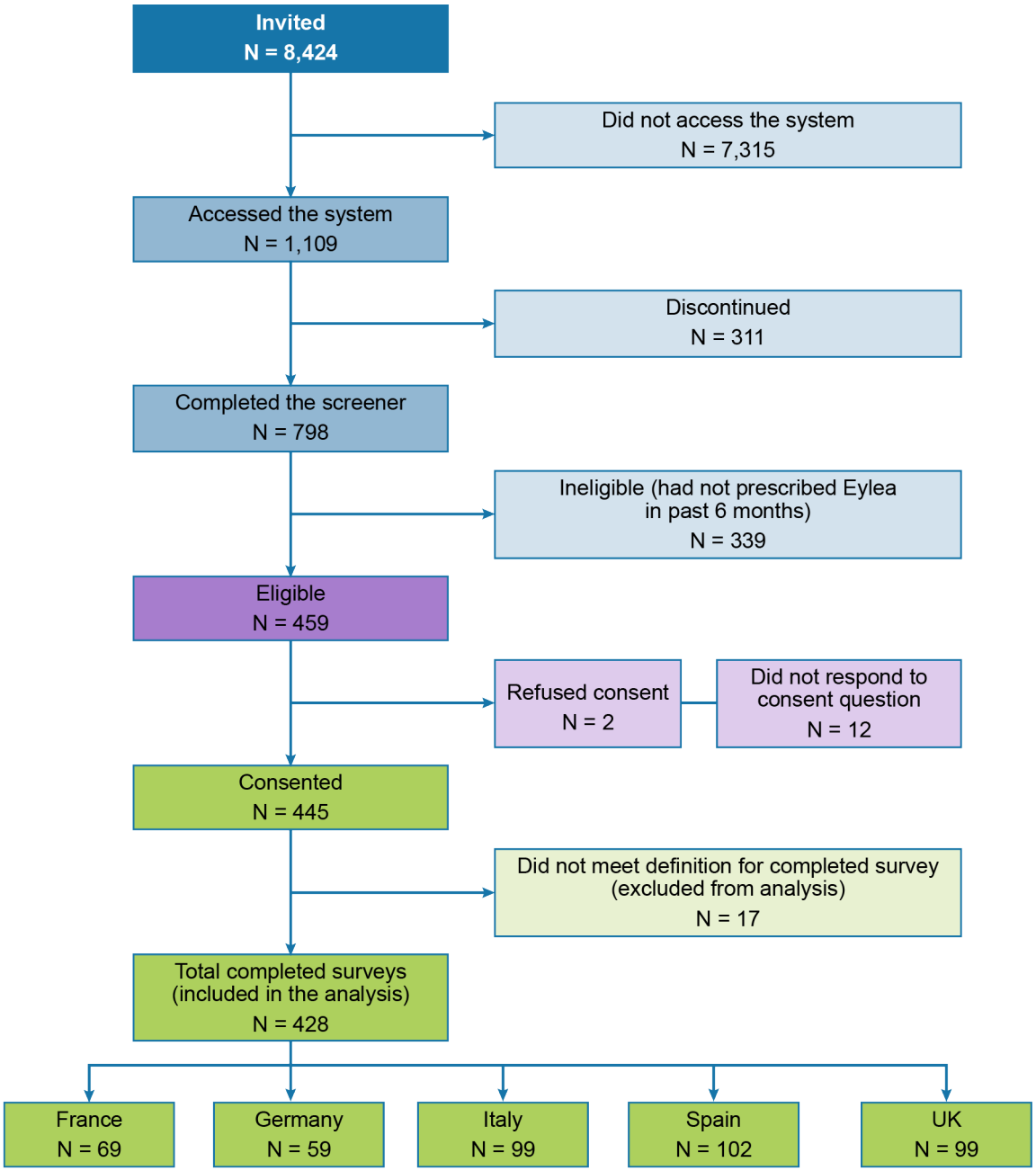
10.1 Physician Assessment Results

10.1.1 Participants

A total of 8,424 physicians were invited to participate in the survey. Of those, 798 completed the screener. Of the physicians who completed the screener, 459 were eligible while the remaining 339 were ineligible because they had not prescribed aflibercept in the preceding 6 months. Of the 459 eligible, 14 did not consent to participate and 17 did not meet the definition for a completed questionnaire (i.e., did not answer at least one knowledge question). The remaining 428 physicians completed the questionnaire and are included in this analysis. The overall response rate was 5.1%. Response rates for physician surveys are traditionally low, and the response rate for this study is somewhat artificial because responses were not allowed once country quotas for responders were met; thus the true response rate, although unmeasurable, would be higher.

Figure 1 presents the disposition of physicians invited to participate.

Figure 1. Disposition of Physician Invited to Participate



UK = United Kingdom.

10.1.2 Descriptive Data

Physicians were asked to indicate their focus within ophthalmology and their responses included retina (74%), general ophthalmology (54%), glaucoma (35%), and cataract (45%). Physicians' most commonly reported having been treating patients for 6-10 years (29%), 11-15 years (19%) and 16-20 years (20%). About three quarters of the physicians (73%) were male.

Table 1 provides characteristics of the participating physicians.

Table 1. Physician Characteristics

Question	France n = 69	Germany n = 59	Italy n = 99	Spain n = 102	UK n = 99	Overall N = 428
		Number of Physicians (%)				
Focus within ophthalmology [a]						
Retina	50 (72)	45 (76)	67 (68)	79 (77)	77 (78)	318 (74)
General ophthalmology	36 (52)	43 (73)	50 (51)	48 (47)	52 (53)	229 (54)
Glaucoma	24 (35)	26 (44)	31 (31)	43 (42)	26 (26)	150 (35)
Cataract	30 (43)	32 (54)	36 (36)	50 (49)	46 (46)	194 (45)
Other	2 (3)	3 (5)	9 (9)	13 (13)	9 (9)	36 (8)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
Years treating patients						
5 years or less	8 (12)	0 (0)	19 (19)	9 (9)	9 (9)	45 (11)
6 to 10 years	19 (28)	12 (20)	32 (32)	29 (28)	31 (31)	123 (29)
11 to 15 years	14 (20)	15 (25)	11 (11)	21 (21)	21 (21)	82 (19)
16 to 20 years	17 (25)	12 (20)	15 (15)	27 (26)	15 (15)	86 (20)
21 to 25 years	5 (7)	10 (17)	6 (6)	7 (7)	12 (12)	40 (9)
More than 25 years	5 (7)	9 (15)	13 (13)	6 (6)	9 (9)	42 (10)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
Sex						
Male	53 (77)	45 (76)	78 (79)	54 (53)	81 (82)	311 (73)
Female	15 (22)	13 (22)	18 (18)	45 (44)	16 (16)	107 (25)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)

UK = United Kingdom.

[a] This was a “tick all that apply” question; thus, the sum of responses can be greater than 100%.

Per the screening criteria, all physicians had prescribed (91%) and/or administered (83%) aflibercept in the past six months for indications including: wAMD (97%), visual impairment due to DME (79%), visual impairment due to macular oedema secondary to CRVO (67%), and visual impairment due to macular edema secondary to BRVO (58%). About half of physicians (52%) reported administering an average of 5 to 40 anti-VEGF injections per month, and a third of physicians (33%) reported administering more than 40 aflibercept injections per month. Most physicians (79%) had administered their last aflibercept injection less than 1 month ago.

Table 2 provides information on physicians' experience with aflibercept.

Table 2. Physicians' Experience With Aflibercept

Question		Number of Physicians (%)				
	France n = 69	Germany n = 59	Italy n = 99	Spain n = 102	UK n = 99	Overall N = 428
Prescribed and/or administered aflibercept in the past 6 months						
Prescribed aflibercept	66 (96)	54 (92)	84 (85)	93 (91)	93 (94)	390 (91)
Administered an aflibercept injection	62 (90)	48 (81)	67 (68)	93 (91)	85 (86)	355 (83)
Indications for which prescribed and/or administered aflibercept						
wAMD	67 (97)	58 (98)	94 (95)	100 (98)	97 (98)	416 (97)
CRVO	61 (88)	49 (83)	41 (41)	62 (61)	73 (74)	286 (67)
DME	64 (93)	51 (86)	63 (64)	90 (88)	72 (73)	340 (79)
BRVO	54 (78)	45 (76)	37 (37)	58 (57)	53 (54)	247 (58)
Other indication	4 (6)	6 (10)	2 (2)	16 (16)	3 (3)	31 (7)
Average monthly anti-VEGF intravitreal injections						
Less than 5 per month	5 (7)	2 (3)	15 (15)	6 (6)	15 (15)	43 (10)
5 to 40 per month	38 (55)	24 (41)	56 (57)	63 (62)	41 (41)	222 (52)
More than 40 per month	23 (33)	31 (53)	20 (20)	29 (28)	40 (40)	143 (33)
I don't know	2 (3)	1 (2)	5 (5)	1 (1)	1 (1)	10 (2)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
Last aflibercept injection administered						
Less than 1 month ago	61 (88)	53 (90)	71 (72)	83 (81)	69 (70)	337 (79)
1 to 6 months ago	4 (6)	3 (5)	18 (18)	16 (16)	23 (23)	64 (15)
I don't know	3 (4)	2 (3)	7 (7)	0 (0)	5 (5)	17 (4)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)

BRVO = branch retinal vein occlusion; CRVO = central retinal vein occlusion; DME = diabetic macular edema; UK = United Kingdom; VEGF = vascular endothelial growth factor; wAMD = wet age-related macular degeneration.

As described in Section 9.9.2.1, the physician knowledge questions were stratified by two variables to evaluate whether there were variations in knowledge among subgroups. Table 3 presents both of those stratification variables and the distribution of responses overall and by country. Discussion of the results for these variables is included in the relevant results sections below.

Table 3. Stratification Variables for Physicians

Category		Number of Physicians (%)				
	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Physician experience with Prescriber Guide						
Reviewed	47 (68)	45 (76)	65 (66)	57 (56)	70 (71)	284 (66)
Received, Did Not Review	10 (14)	11 (19)	6 (6)	8 (8)	11 (11)	46 (11)
Did Not Receive	10 (14)	2 (3)	25 (25)	33 (32)	16 (16)	86 (20)
Skipped	2 (3)	1 (2)	3 (3)	4 (4)	2 (2)	12 (3)
Person with primary responsibility for preparation of aflibercept injections at site						
I am responsible	55 (80)	33 (56)	45 (45)	36 (35)	64 (65)	233 (54)
A specialized nurse	9 (13)	19 (32)	48 (48)	16 (16)	32 (32)	124 (29)
Pharmacy	1 (1)	5 (8)	3 (3)	50 (49)	3 (3)	62 (14)
Laboratory	2 (3)	0 (0)	1 (1)	0 (0)	0 (0)	3 (1)
Other	2 (3)	2 (3)	2 (2)	0 (0)	0 (0)	6 (1)

UK = United Kingdom.

Note: A stratification variable was derived based on responses to question 23 (“Have you received the material?” and “Have you reviewed the material?”). The categories for this stratification are 1) “reviewed,” 2) “received, but did not review,” and 3) “did not receive.” Table 3 presents the results for this stratification variable.

Table 6 presents the proportion of physicians who responded “Yes” to “Have you received the material?” and “Yes” to “Have you reviewed the material?” directly, as asked in question 23.

10.1.3 Outcome Data

Not applicable.

10.1.4 Main Results

In the following sections, we present key results from physicians who completed the questionnaire. The results are organised in the following categories: (1) physician knowledge, (2) receipt and use of aflibercept educational materials, (3) ratings of aflibercept education materials, and (4) use of patient booklet.

First, we describe the results for the overall sample, then results stratified by country and physician experience with the Eylea Prescriber Guide. Results from questions about storage and preparation are also stratified and described by who has the primary responsibility for preparing the injection at their site. However, we do not discuss the categories "Laboratory" (N = 3) or "Other" (N = 6), as these strata are too small to provide meaningful information.

Annex 5 includes tables presenting the complete set of knowledge question results for physicians overall and by country. Annex 6 includes tables presenting results by other stratification variables. These results are broken into those stratified by prescriber guide and those stratified by person with primary responsibility of preparing the injection.

10.1.4.1 Physician Knowledge

Storage and Preparation

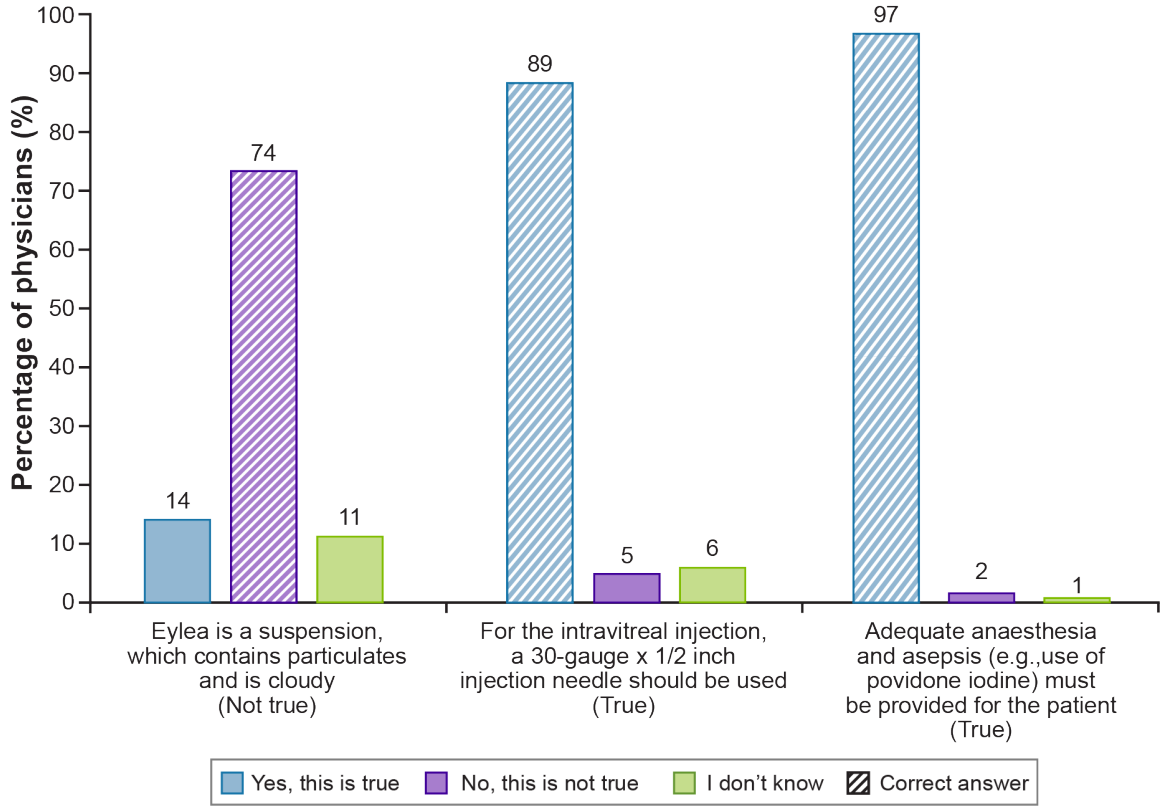
Seventy-four percent of physicians correctly identified the incorrect statement "Eylea is a suspension, which contains particulates and is cloudy"; 89% correctly responded that a "30-gauge x ½ inch injection needle should be used"; and 97% correctly responded that "adequate anaesthesia and asepsis must be provided for the patient" (Figure 2). Sixty-seven percent selected the correct response to all three questions.

Knowledge on these questions was similar across countries, with the exception of Spain where physicians scored somewhat higher; 82% of physicians in Spain responded correctly to all three questions, compared to 59%-68% for the physicians from the other countries (Annex 5, Table 3-1; Questions 1a, 1h, and 1i).

There were small differences in the proportion of correct responses to these questions between physicians who reviewed the prescriber guide, those who had received but did not review it, and those who did not receive it (Annex 6, Table 3-1a; Questions 1a, 1h, and 1i).

Physicians from sites reporting "A specialized nurse" as having the primary responsibility of preparing the injection had a lower proportion who selected the correct response to all three questions (62% correct) than groups reporting "I am responsible" (69%) or the "Pharmacy" is responsible (74%) (Annex 6, Table 3-1b; Questions 1a, 1h, and 1i).

Figure 2. For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Question 1a, 1h, 1i) (N = 428)



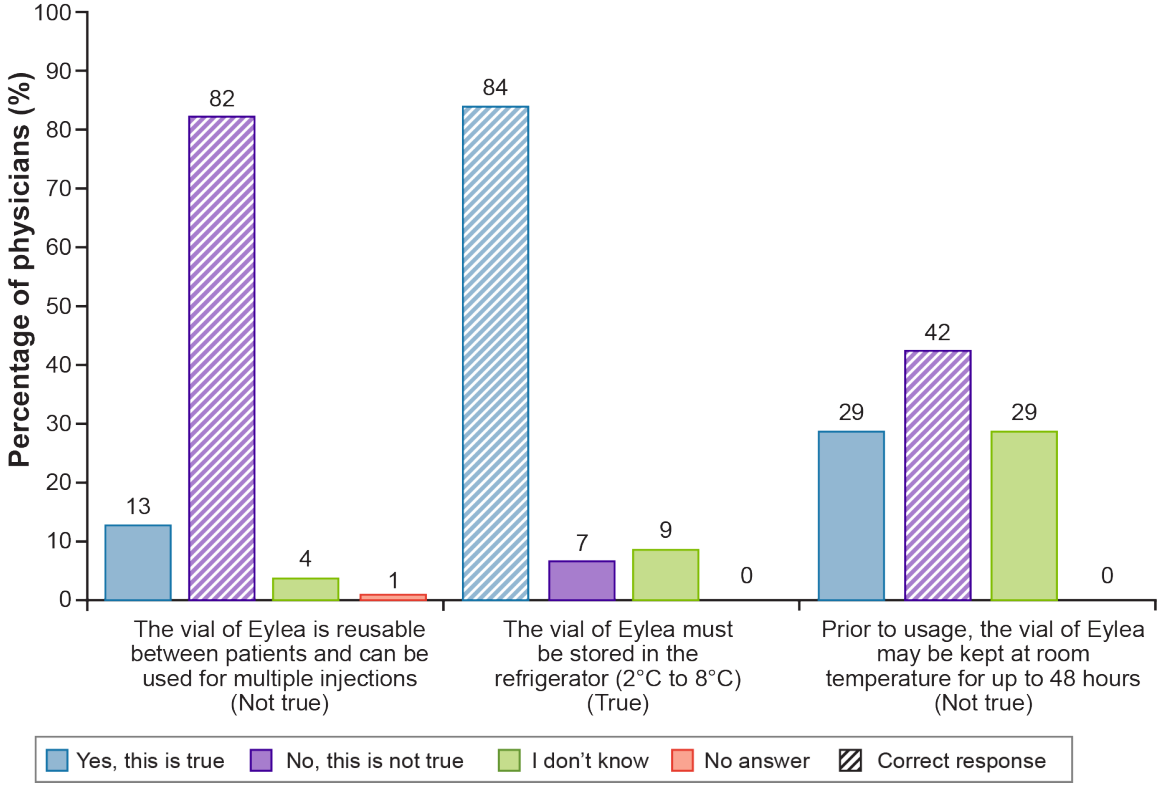
Eighty-two percent of physicians correctly identified that the statement "the vial of Eylea is reusable between patients and can be used for multiple injections" as false; 84% correctly responded that the vial should be stored in the refrigerator; and 42% correctly identified the statement "prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours" as inaccurate (the actual duration is up to 24 hours) (Figure 3). Thirty-three percent selected the correct response to all three questions.

Physician knowledge was similar across countries for the question regarding whether the vial was reusable between patients (88%-95% correct), with the exception of Spain (53%). Knowledge across countries was also similar for the question regarding whether the vial should be stored in the refrigerator (83%-90%), with the exception of the UK (73%). Physicians from the UK (52% correct) and Germany (50%) more often identified the inaccurate statement about whether the vial may be kept at room temperature for up to 48 hours than physicians from the other countries (33-38%) did (Annex 5, Table 3-1; Questions 1c, 1e, and 1g).

There were small differences in the proportion of correct responses to these questions between physicians who reviewed the prescriber guide, those who had received but did not review it, and those who did not receive it (Annex 6, Table 3-1a; Questions 1c, 1e, and 1g).

Knowledge was similar across groups for who has primary responsibility of preparing the injection. The most notable difference was in response to whether the vial was reusable, where knowledge ranged from 45% for the pharmacy group to 92% correct for the specialised nurse group (Annex 6, Table 3-1b; Questions 1c, 1e, and 1g).

Figure 3. For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Question 1c, 1e, 1g) (N = 253)[a]



[a] Due to the inclusion of questions about the prefilled syringe, which was not actually available at the time of the survey, some physicians erroneously indicated they used only the prefilled syringe and were not allowed to respond to these questions as part of a skip pattern.

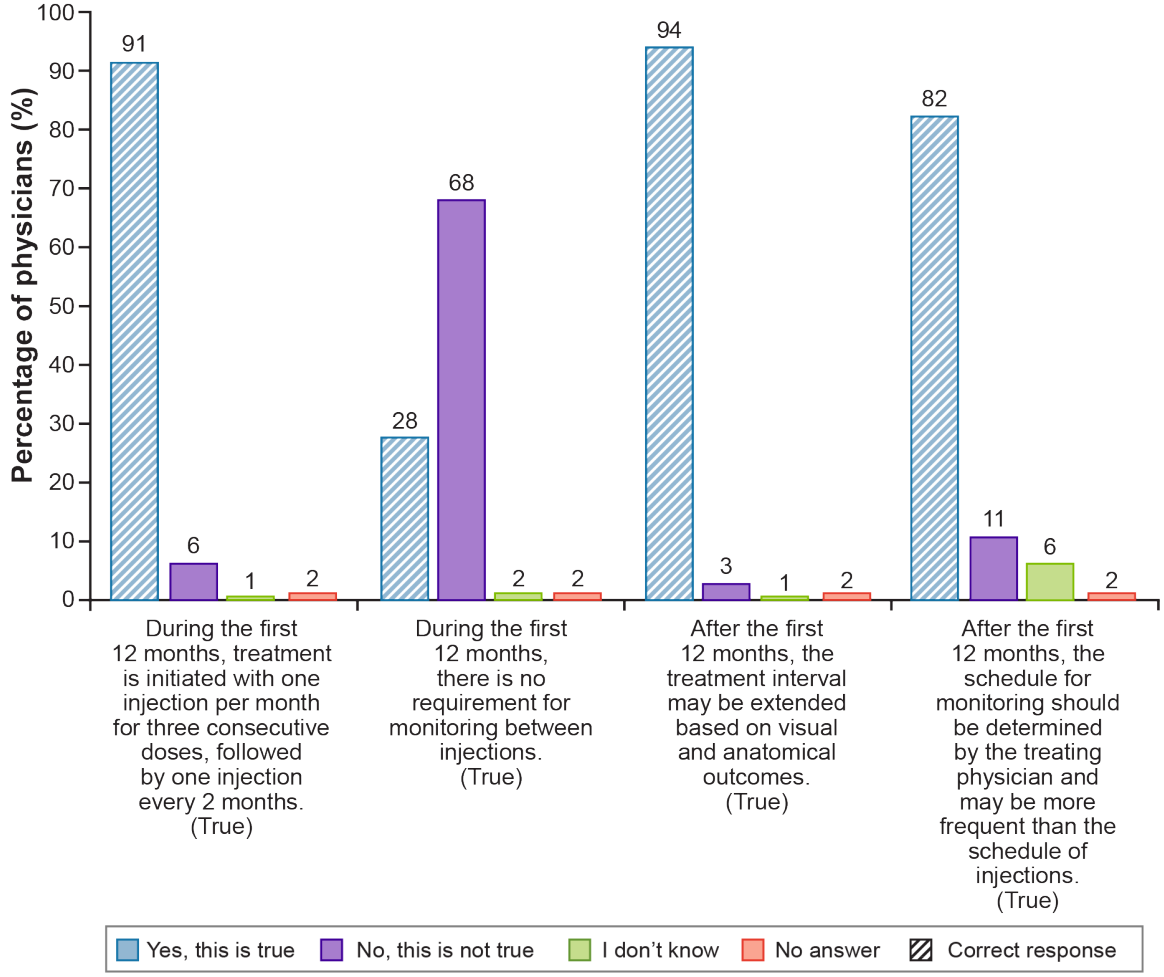
Dosing and Monitoring

Dosing for wAMD

Physicians were presented with four true/false statements concerning dosing recommendations for wAMD during and after the first 12 months (Figure 4). The 416 physicians who prescribed and/or administered aflibercept in the past 6 months for wAMD were asked to indicate whether each statement was true or false. Each of the four statements was in fact true, and the following are the percentage of physicians who correctly identified each as true: "treatment is initiated with one injection per month for three consecutive doses, followed by one injection every 2 months" (91%), "there is no requirement for monitoring between injections" (28%), "the treatment interval may be extended based on visual and anatomical outcomes" (94%), and "the schedule for monitoring should be determined by the treating physician and may be more frequent than the schedule of injections" (82%) (Annex 5, Table 3-2; Question 3).

The proportion of correct responses to these questions among physicians was similar across countries and across levels of experience with the prescriber guide (Annex 6, Table 3-2a; Question 3).

Figure 4. For each of the following statements related to the Eylea dosing and monitoring recommendations for the treatment of wAMD, please indicate if the statement is true, not true, or if you do not know. (Question 3) (N = 416)

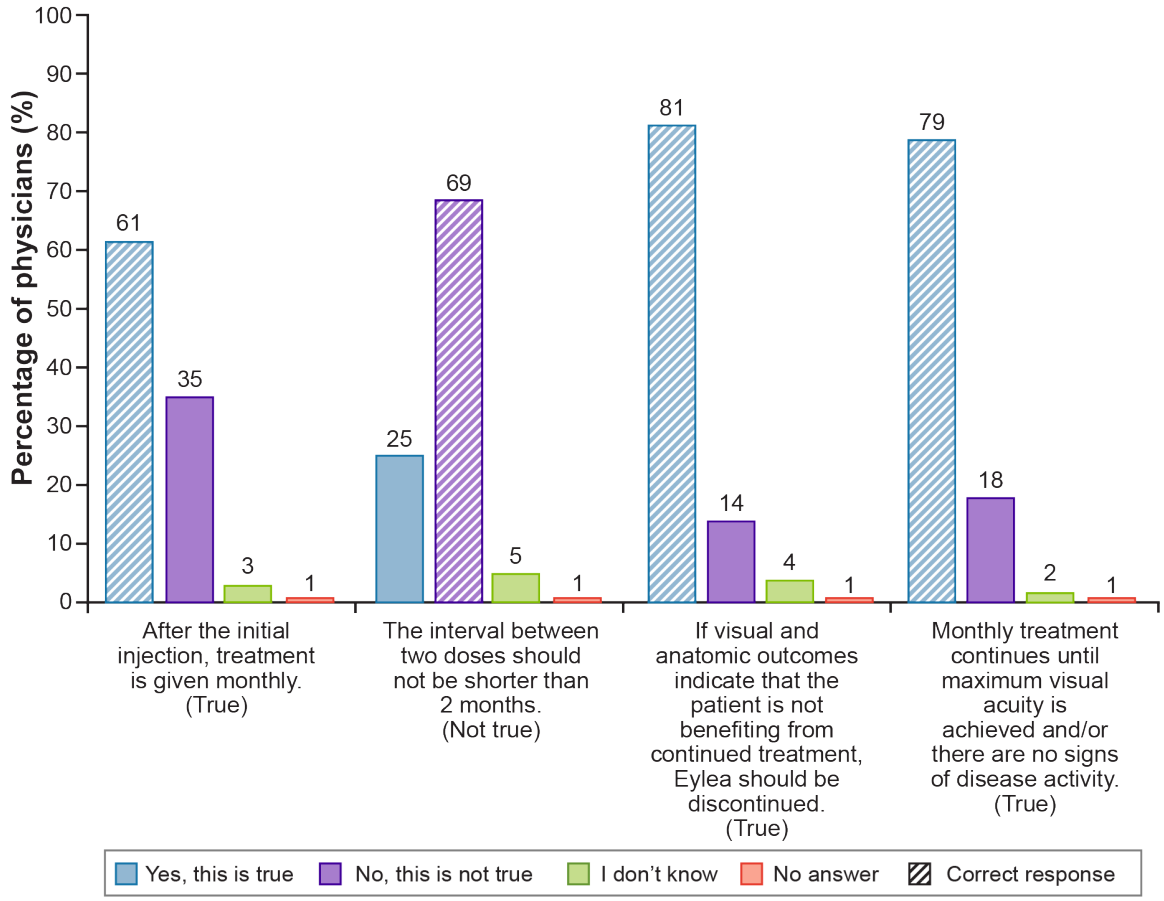


Dosing for CRVO and BRVO

Physicians were presented with four true/false statements concerning dosing recommendations for CRVO or BRVO (Figure 5). These were asked only of the 307 physicians who prescribed and/or administered aflibercept in the past six months for CRVO or BRVO. Overall, the following are the proportions of physicians who correctly identified each of the following three statements as true: "After the initial injection, treatment is given monthly" (61%), "If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued" (81%), and "Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity" (79%). Sixty-nine percent of physicians correctly identified the statement "the interval between two doses should not be shorter than 2 months" as false (Annex 5, Table 3-2; Question 4).

The proportion of correct responses across countries and by experience with the prescriber guide were similar for this question (Annex 6, Table 3-2a; Question 4).

Figure 5. For each of the following statements related to the Eylea dosing recommendations for the treatment of macular oedema secondary to CRVO or BRVO, please indicate if the statement is true, not true, or if you do not know. (Question 4) (N = 307)

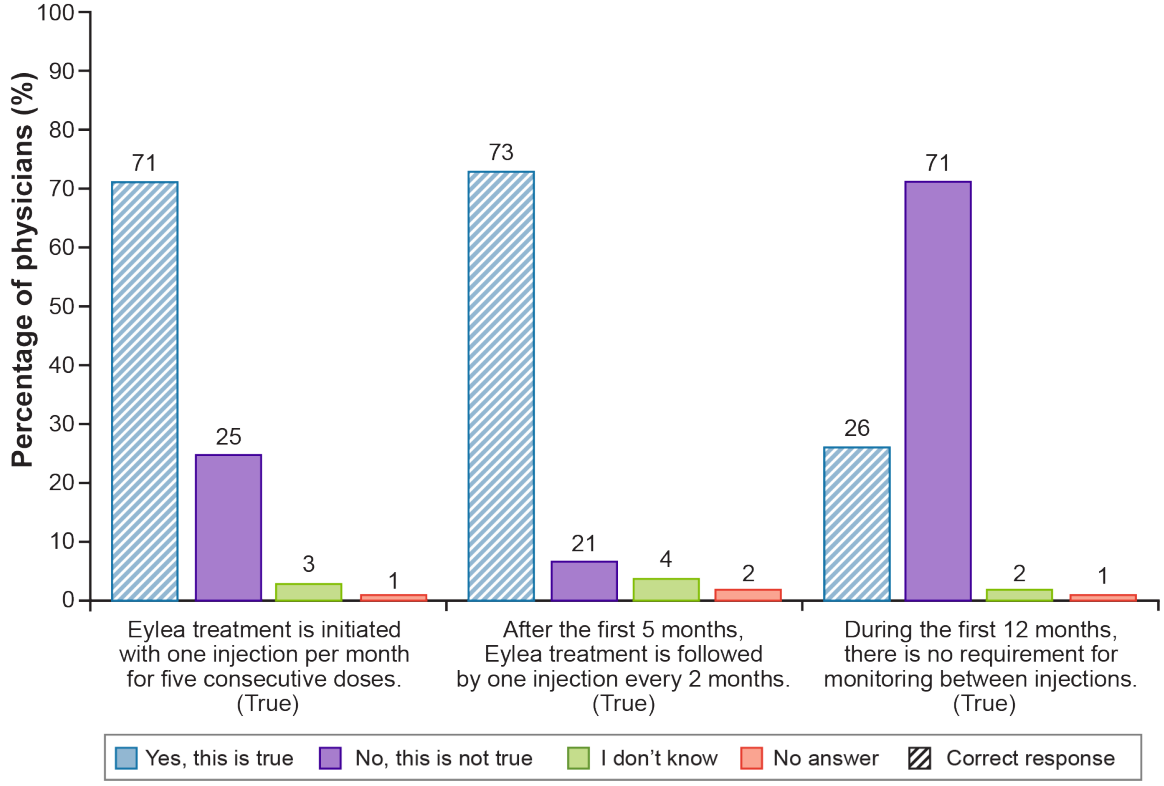


Dosing for DME

Physicians were presented with three true/false questions concerning dosing recommendations for DME (Figure 6). These were asked only of the 340 physicians who prescribed and/or administered aflibercept in the past six months for DME. Overall, the following are the proportions of physicians that correctly identified each of the three statements as true: "Eylea treatment is initiated with one injection per month for five consecutive doses" (71%), "After the first 5 months, Eylea treatment is followed by one injection every two months" (73%), and "During the first 12 months, there is no requirement for monitoring between injections" (26%) (Annex 5, Table 3-2; Question 5).

The proportion of correct responses across countries and by experience with the prescriber guide were similar for this question (Annex 6, Table 3-2a; Question 5).

Figure 6. For each of the following statements related to the Eylea dosing recommendations for the treatment of DME, please indicate if the statement is true, not true, or if you do not know. (Question 5) (N = 340)



Recommended Dose for Aflibercept

Most physicians (73%) correctly responded that 50 microlitres was the recommend dose for aflibercept (Table 4). The proportion of correct response varied across countries with Germany and the UK having the highest at 83%, and the other countries ranged from 66% to 69%. The proportion of correct responses for those who reviewed the prescriber guide (78%) was slightly higher than for those who received but did not review it (67%) and did not receive it (63%) (Annex 6, Table 3-2a; Question 2).

Table 4. Recommended Dose for Aflibercept

Question	Number of Physicians (%)					
	France n = 69	Germany n = 59	Italy n = 99	Spain n = 102	UK n = 99	Overall N = 428
What is the recommended dose for Eylea?						
12.5 microlitres (0.5 mg)	9 (13)	3 (5)	18 (18)	24 (24)	13 (13)	67 (16)
50 microlitres (2 mg)[a]	47 (68)	49 (83)	68 (69)	67 (66)	82 (83)	313 (73)
90 microlitres (3.6 mg)	0 (0)	2 (3)	1 (1)	1 (1)	1 (1)	5 (1)
100 microlitres (4 mg)	6 (9)	3 (5)	3 (3)	3 (3)	1 (1)	16 (4)
I don't know	7 (10)	2 (3)	7 (7)	7 (7)	1 (1)	24 (6)
No answer	0 (0)	0 (0)	2 (2)	0 (0)	1 (1)	3 (1)

[a] Correct response

Excess Volume of Aflibercept

Eighty-seven percent correctly identified the statement "the vial contains more than the recommend dose of Eylea and excess volume should be expelled before injection" as true. Sixty-seven percent correctly responded that the plunger of the syringe should be depressed until the tip aligns with the 0.05 ml line after removing all of the drug from the aflibercept vial (Table 5).

For the question regarding the vial containing more than the recommended dose, the proportion correct was high (83%-95%) among the physicians from each country, with the exception of Spain, where the proportion correct was slightly lower (75%). Results were similar across levels of physicians' experience with the prescriber guide (Annex 6, Table 3-2a; Question 8).

For the question regarding the tip aligning with the 0.05 ml line, the correct response proportion among physicians from Italy was 52% and ranged from 64% to 76% among physicians from the other countries (Table 5). Physicians who reviewed the prescriber guide had higher correct response proportion (72%) than those who received but did not review it (56%) and those who did not receive it (58%) (Annex 6, Table 3-2a; Question 9).

Table 5. Excess Volume of Aflibercept

Question	Number of Physicians (%)					
	France n = 69	Germany n = 59	Italy n = 99	Spain n = 102	UK n = 99	Overall N = 428
The Eylea vial contains more than the recommended dose of Eylea and excess volume should be expelled before injecting.						
True [a]	47 (94)	31 (91)	35 (83)	48 (75)	60 (95)	221 (87)
False	2 (4)	2 (6)	4 (10)	11 (17)	3 (5)	22 (9)
I don't know	1 (2)	1 (3)	2 (5)	4 (6)	0 (0)	8 (3)
No answer	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	2 (1)
Not applicable skip pattern [b]	19	25	57	38	36	175
After removing all of the drug from the Eylea vial with a syringe, the plunger of the syringe should be depressed until the tip aligns with the line that marks which number of milliliters (ml) on the syringe?						
0.05 ml [a]	33 (66)	26 (76)	22 (52)	41 (64)	48 (76)	170 (67)
0.1 ml	4 (8)	1 (3)	4 (10)	5 (8)	4 (6)	18 (7)
0.15 ml	0 (0)	1 (3)	0 (0)	0 (0)	1 (2)	2 (1)
0.2 ml	4 (8)	3 (9)	4 (10)	2 (3)	1 (2)	14 (6)
0.5 ml	8 (16)	2 (6)	7 (17)	9 (14)	7 (11)	33 (13)
I don't know	1 (2)	1 (3)	4 (10)	6 (9)	2 (3)	14 (6)
No answer	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	2 (1)
Not applicable skip pattern [b]	19	25	57	38	36	175

[a] Correct response

[b] Due to the inclusion of questions about the prefilled syringe, which was not actually available at the time of the survey, some physicians erroneously indicated they used only the prefilled syringe and were not allowed to respond to these questions as part of a skip pattern.

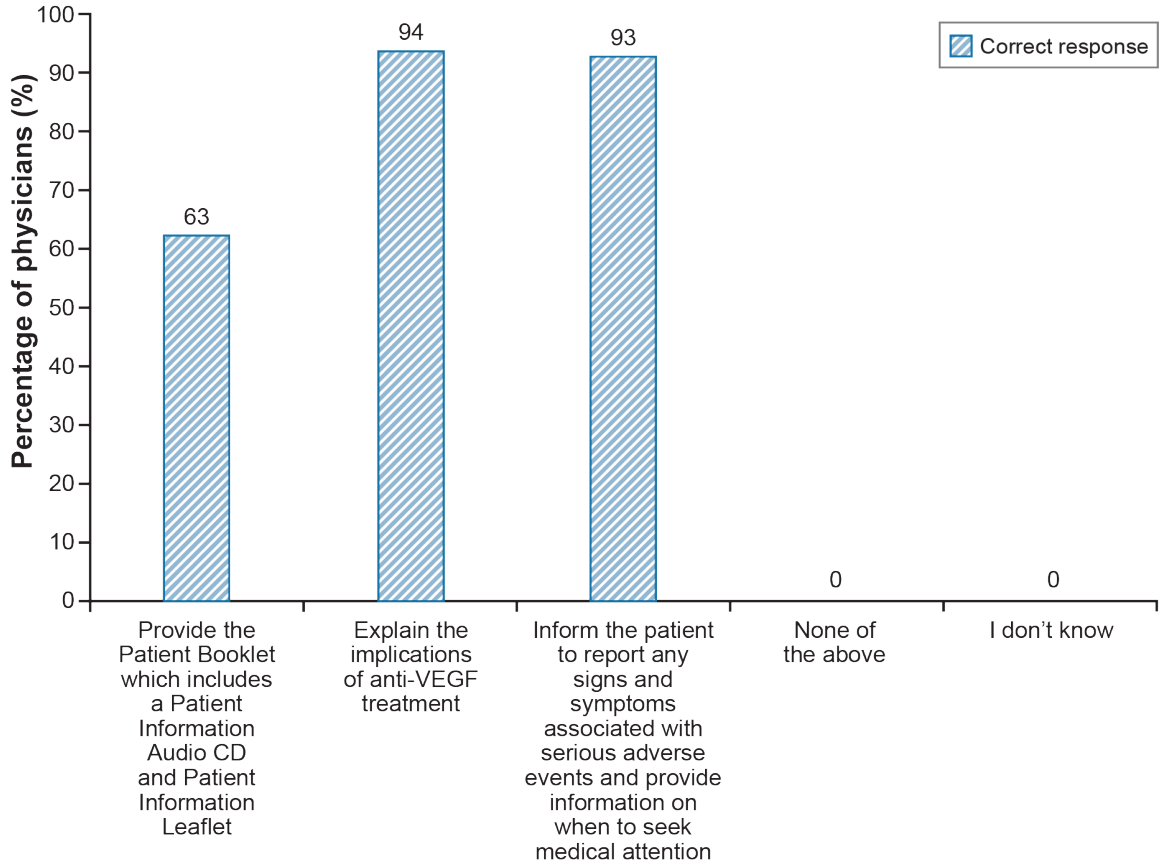
Safe Use

Preparing the Patient for Treatment

Physicians were asked to tick all statements that apply in response to the question, "what should you do to prepare the patient before the start of treatment with Eylea?" (Figure 7). Three correct responses were listed among the options and overall, the proportion correct was highest for "explain the implications of anti-VEGF treatment" (94%) and "inform the patient to report any signs and symptoms…" (93%); a smaller proportion of the physicians selected "provide the patient booklet …" (63%).

Across countries, the correct response percentages were similar for "explain the implications of anti-VEGF treatment" and "inform the patient to report any signs and symptoms…" For the statement "provide the patient booklet …," the proportion of correct responses was consistent across countries (43%-64%) with the exception of the UK where 96% selected the correct response (Annex 5, Table 3-3; Question 10). Across levels of experience with the prescriber guide, the proportion of correct responses was similar for all the three response options (Annex 6, Table 3-3a; Question 10).

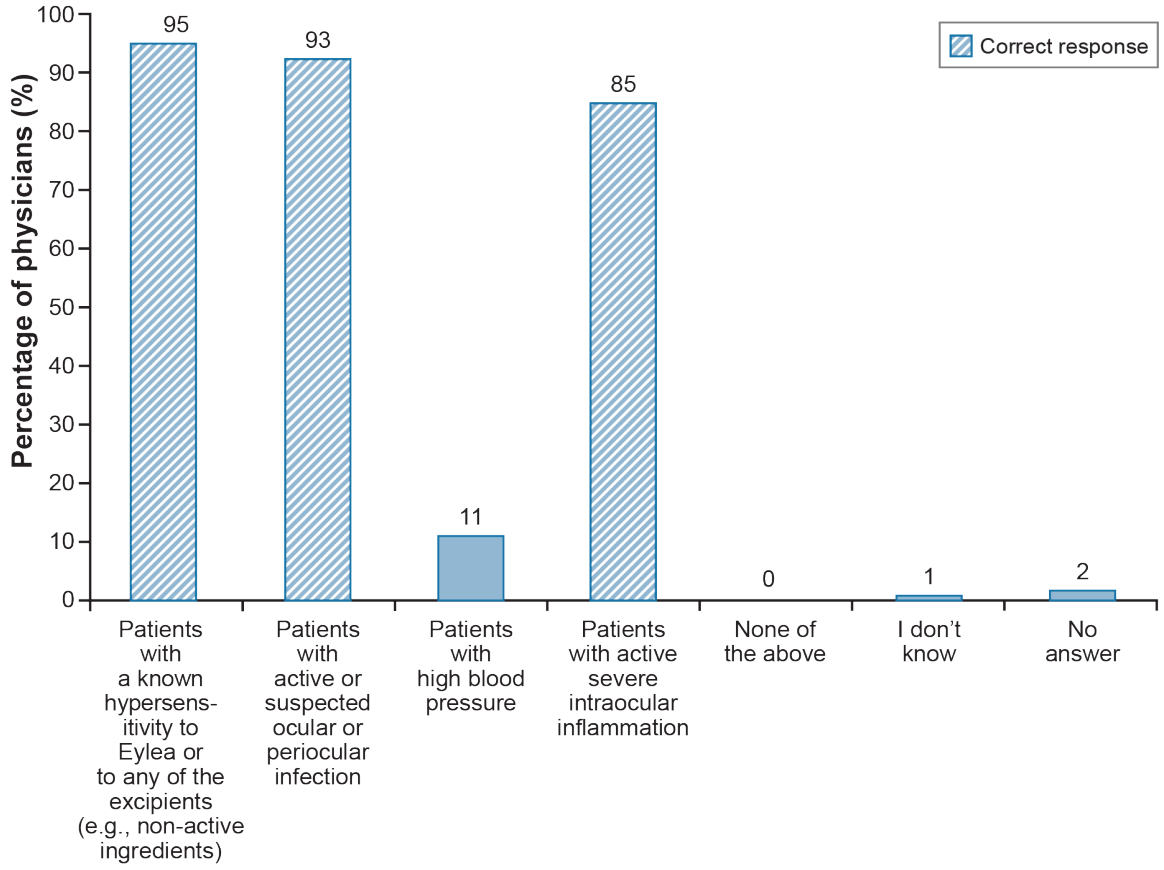
Figure 7. What should you do to prepare the patient before the start of treatment with Eylea? Tick all that apply. (Question 10) (N = 428)



Contraindications

Physicians were asked to identify the contraindications for aflibercept (Figure 8). Overall, knowledge was high with the proportion of correct responses ranging from 85% for "patients with active severe intraocular inflammation" to 95% for hypersensitivity. The proportions of correct responses were similar across countries and by physicians' experience with the guide (Annex 5, Table 3-3; Question 11 and Annex 6, Table 3-3a; Question 11).

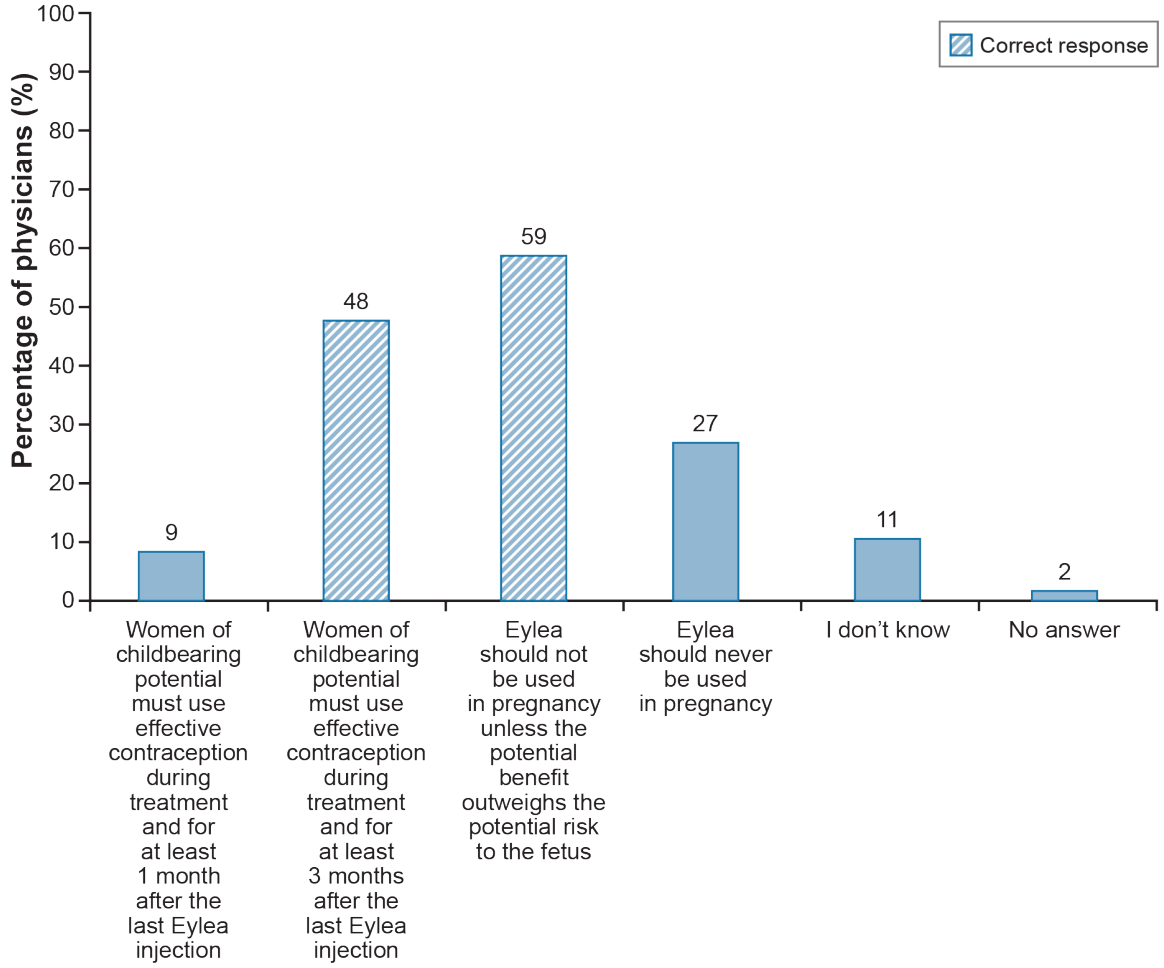
Figure 8. Eylea is contraindicated in which of the following patients? Tick all that apply. (Question 11) (N = 428)



Use in Women of Childbearing Potential

Physicians were asked about the recommended use of aflibercept in women of childbearing potential (Figure 9). Overall, 48% of physicians correctly responded that "women of childbearing potential must use effective contraception …", and 59% correctly reported that "Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk…". There were small differences in the proportion of correct responses across countries; knowledge by physicians' experience with the prescriber guide was similar (Annex 5, Table 3-3; Question 12 and Annex 6, Table 3-3a; Question 12).

Figure 9. What is the recommended use of Eylea in women of childbearing potential? Tick all that apply. (Question 12) (N = 428)



Injection Procedure

Physicians were asked a series of five questions about proper injection procedures (Figure 10 and Figure 11). Overall, physicians' knowledge of this topic was high.

The majority of physicians (94%) correctly confirmed that topical anaesthesia should be used prior to the aflibercept injection. Likewise, 96% of physicians correctly identified the statement "a disinfectant should be applied to the periocular skin, eyelid, and ocular surface" as true. When asked to identify steps that should be taken prior to marking the scleral injection site, a high percentage of the physicians correctly selected "cover the eye with a sterile drape" (86%) and "insert a sterile lid speculum" (88%). Most physicians (83%) correctly responded that the eye should be marked at a distance 3.5 to 4.0 mm posterior to the limbus in preparation for the aflibercept injection. Similarly, most physicians (88%) correctly responded that the injection needle should be inserted into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe.

The proportion of correct responses was similar across countries and by physicians' experience with the prescriber guide for these questions (Annex 5, Table 3-4; Questions 13-17 and Annex 6, Table 3-4a; Questions 13-17).

Figure 10. Questions 13, 14 and 15 (N = 428)

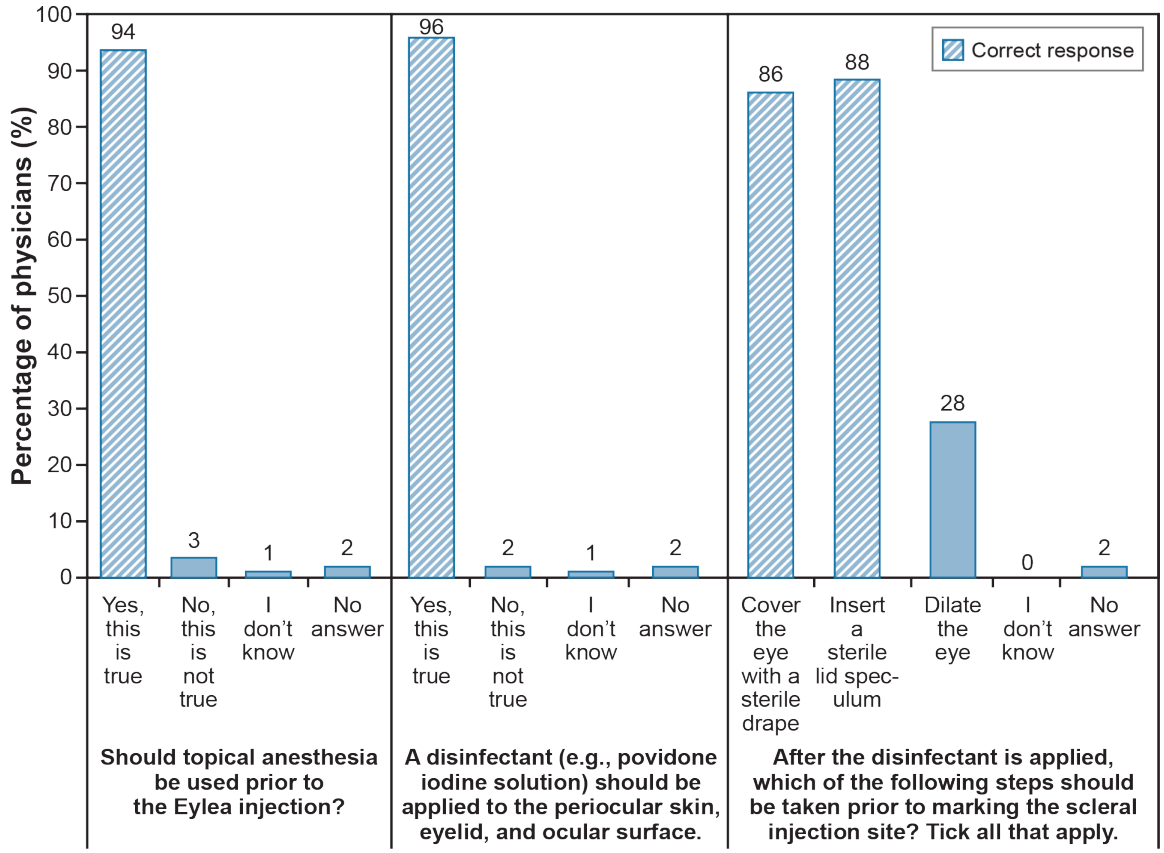
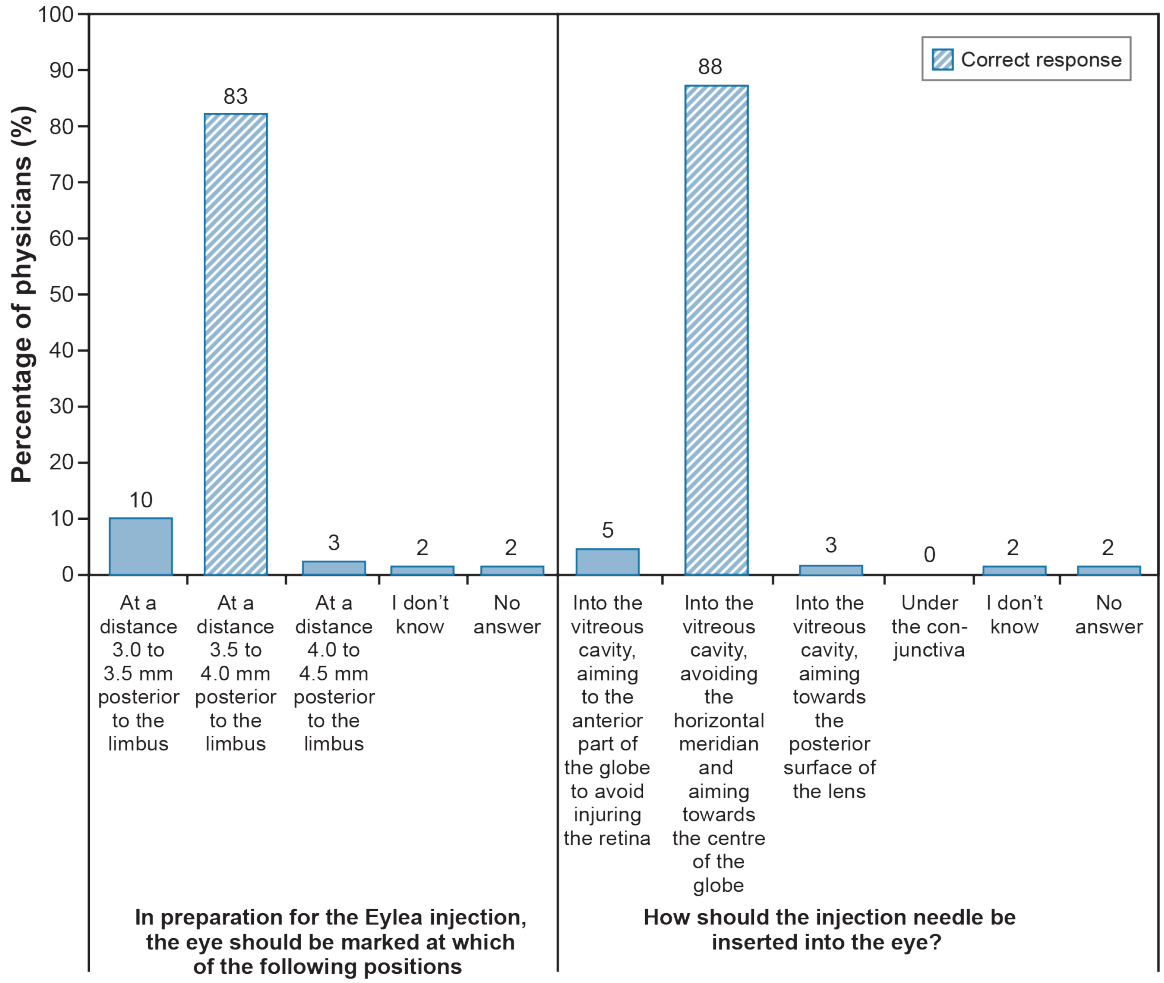


Figure 11. Questions 16 and 17 (N = 428)



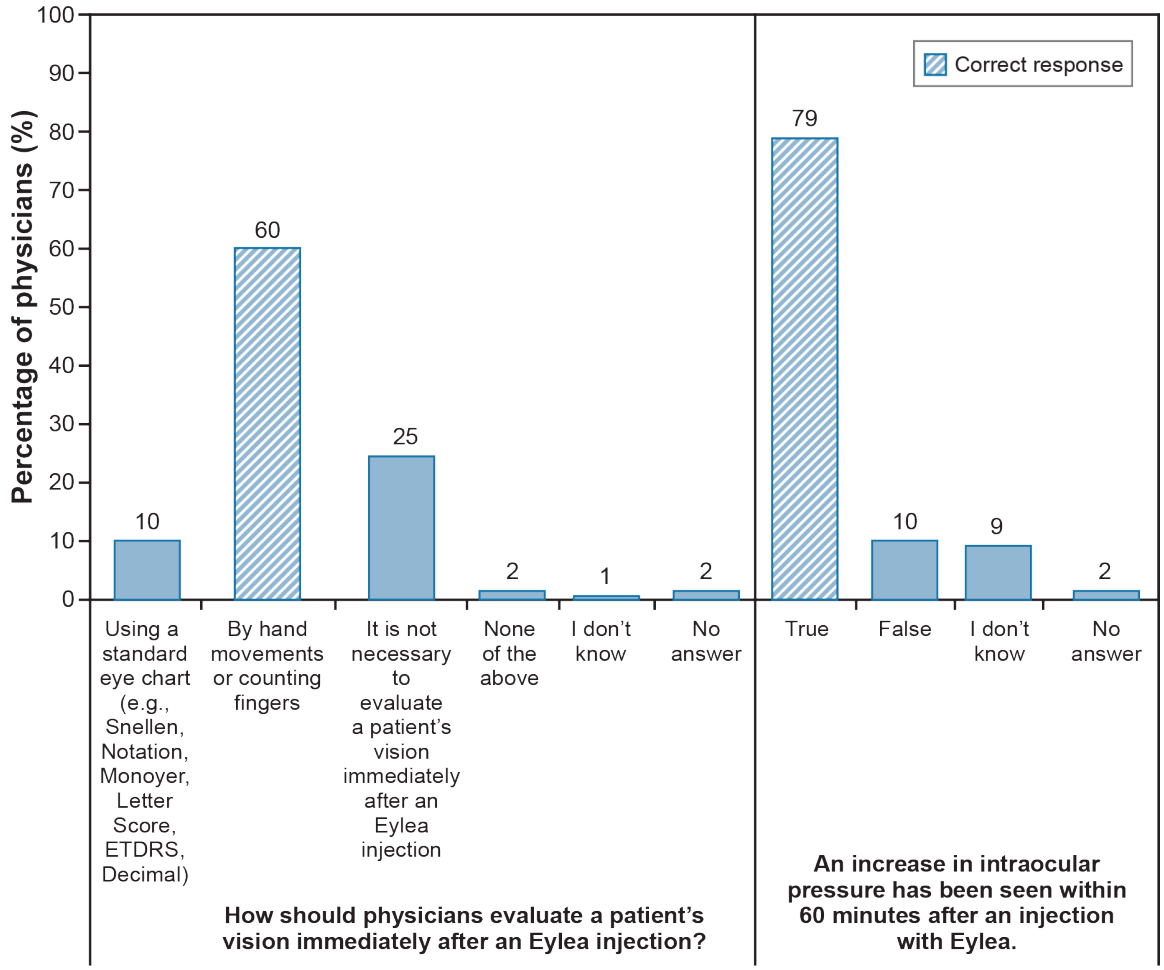
Side Effects

When asked how physicians should evaluate a patient's vision immediately after an aflibercept injection, 60% of physicians correctly responded "by hand movements or counting fingers". There was variability in correct responses across countries with the UK being the highest (82%), followed by Germany (76%), France and Spain (both 61%), and Italy (26%) (Annex 5, Table 3-5; Question 18). The proportion of correct responses was similar for physicians who had reviewed the prescriber guide or received it but did not review it (64% and 65% respectively) but lower for those physicians who did not receive it (47%) (Annex 6, Table 3-5a; Question 18).

Most physicians (79%) correctly identified the statement "an increase in intraocular pressure has been seen within 60 minutes after an injection with Eylea" as true. The proportion of correct responses was high (65%-92%) across countries (Annex 5, Table 3-5; Question 19). The proportion of correct responses was high for those physicians who had reviewed the prescriber guide and received it but did not review it (83% and 89% respectively), but lower for those who did not receive it (69%) (Annex 6, Table 3-5a; Question 19).

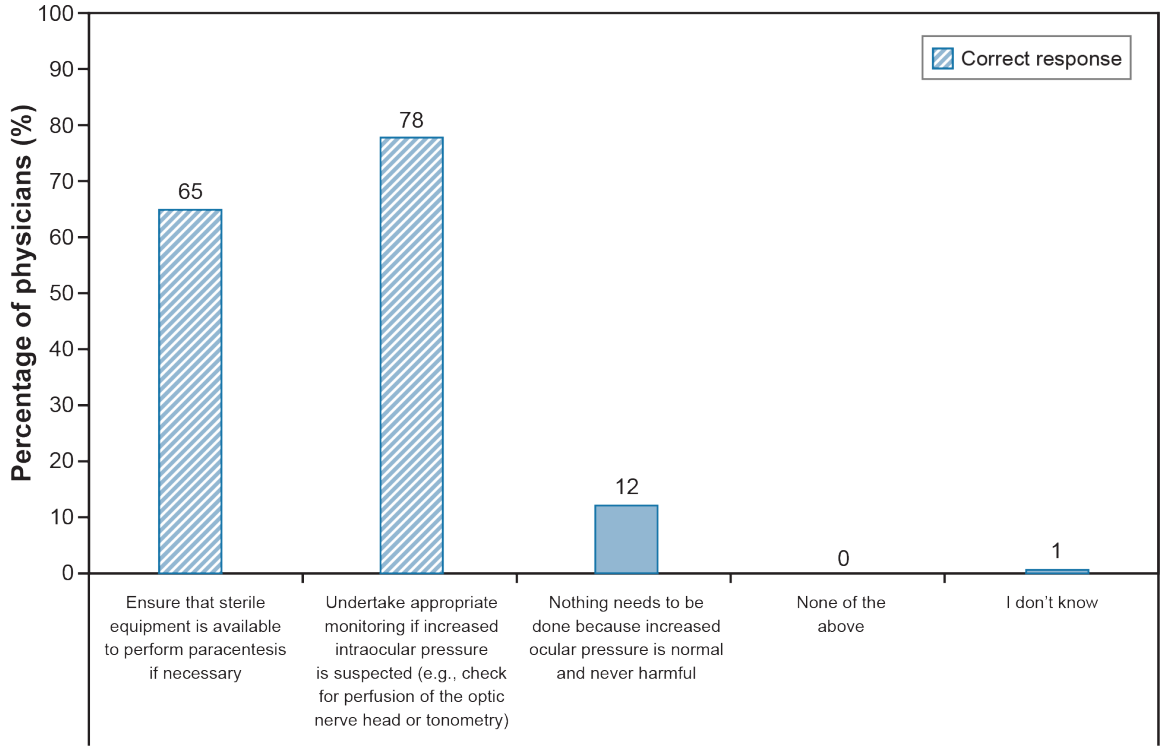
Figure 12 presents responses to these questions.

Figure 12. Questions 18 and 19 (N = 428)



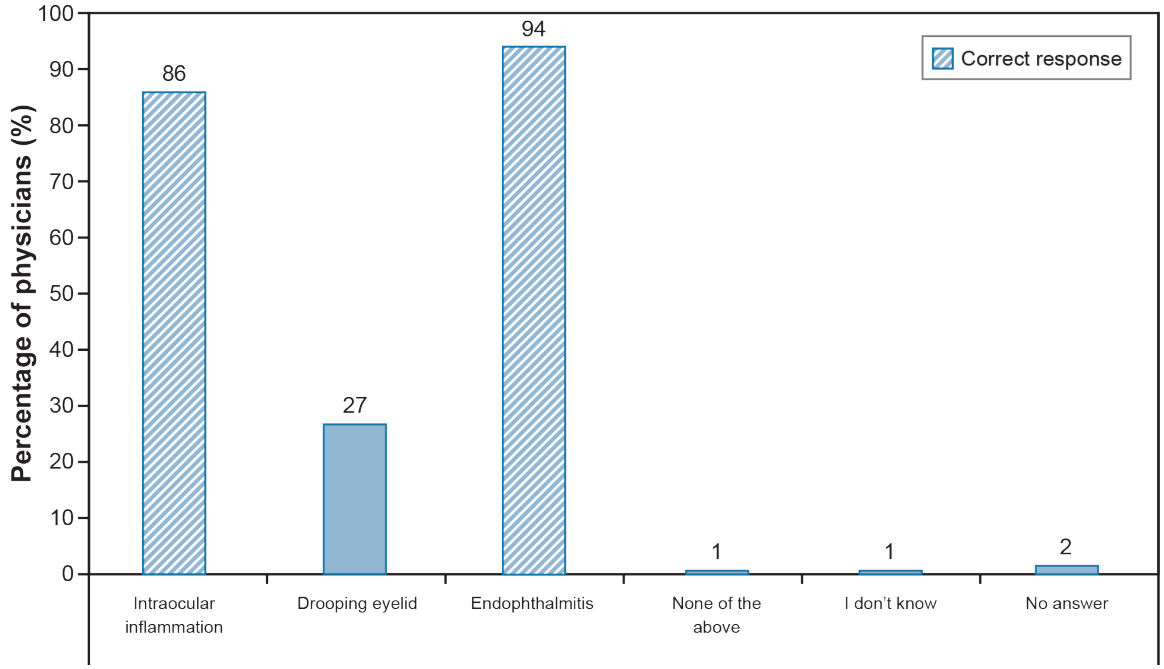
Physicians were asked what they should do "in relation to the potential of increased intraocular pressure immediately following an Eylea injection" (Figure 13). Sixty-five percent of physicians correctly responded "ensure that sterile equipment is available to perform paracentesis, if necessary," and 78% of physicians correctly responded "undertake appropriate monitoring if increased intraocular pressure is suspected (e.g., check for perfusion of the optic nerve head or tonometry)." Across countries, knowledge was similar for both responses, except for France, which was relatively low (42% and 46%, respectively) (Annex 5, Table 3-5; Question 20). There was minimal variation in physicians' knowledge of these topics by their experience with the prescriber guide (Annex 6, Table 3-5a; Question 20).

Figure 13. What should physicians do in relation to the potential of increased intraocular pressure immediately following an Eylea injection? Tick all that apply. (Question 20) (N = 428)



Physicians were asked to tick all statements that apply in response to the question, "after the Eylea injection, patients should be instructed to report any symptoms and suggestive of which of the following conditions" (Figure 14) Overall, a high proportion of physicians correctly ticked "intraocular inflammation" (86%) and "endophthalmitis" (94%). Knowledge was consistently high across countries and by physicians' experience with the prescriber guide (Annex 5, Table 3-5; Question 21 and Annex 6, Table 3-5a; Question 21).

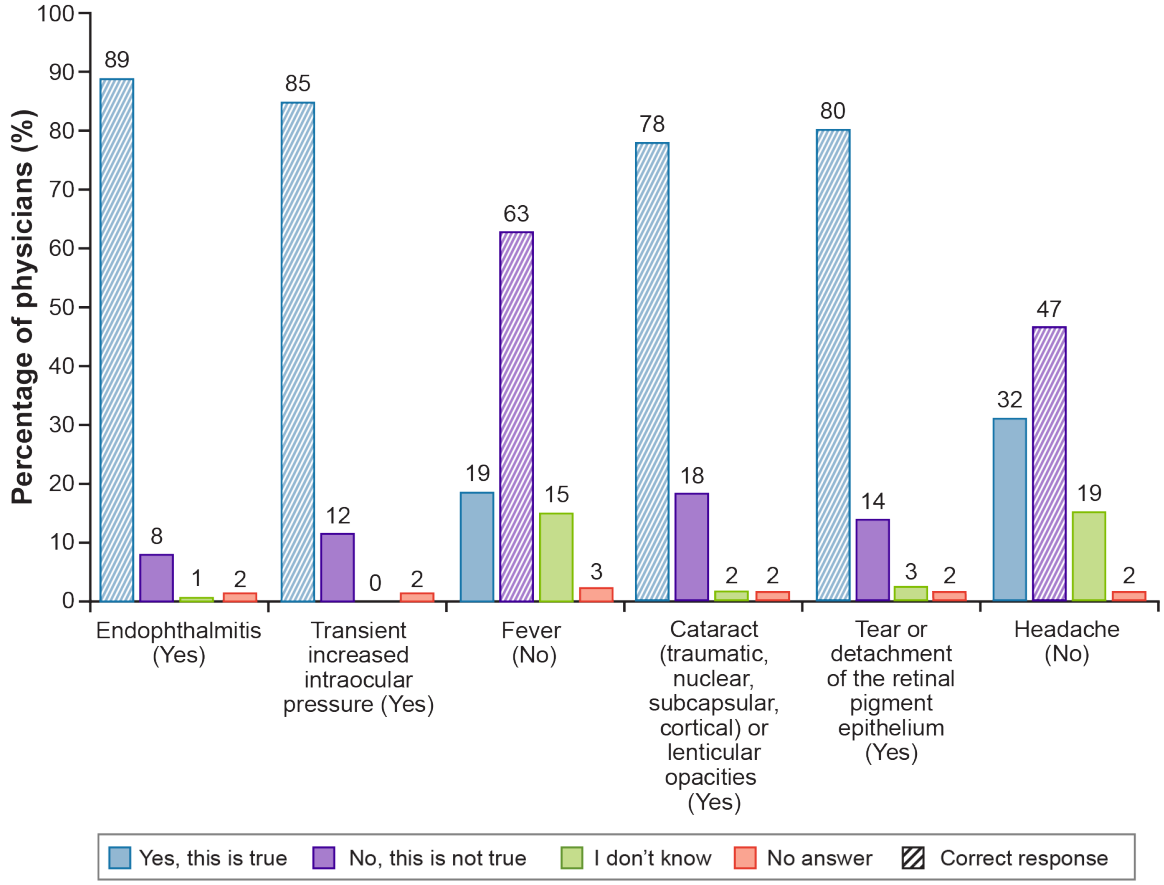
Figure 14. After the Eylea injection, patients should be instructed to report any symptoms suggestive of which of the following conditions? Tick all that apply. (Question 21) (N = 428)



Physicians were given a list of potential signs or symptoms that are known undesirable side effects of aflibercept injection (Figure 15), and each of the potential signs or symptoms was correctly selected by at least 78% of physicians: endophthalmitis (89%), transient increased intraocular pressure (85%), cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities (78%), and retinal tear or retinal detachment (80%). Fewer physicians correctly identified that fever (63%) and headache (47%) were not potential related side effects.

The proportion of correct responses for this question was similar across countries, except when identifying cataract and tear or detachment of the retinal pigment epithelium. The proportion of correct responses in France (67% and 68% respectively) and Italy (71% for both items) were lower than for other countries (78%-88% and 86%-88% respectively) (Annex 5, Table 3-5; Question 22). The proportion of correct responses by physicians was similar across countries for identifying effects not undesirable. The proportion of correct responses was similar across levels of experience with the prescriber guide (Annex 6, Table 3-5a; Question 22).

Figure 15. Which of the following signs or symptoms are known undesirable side effects of using Eylea? (Question 22) (N = 428)



10.1.4.2 Physician Receipt and Use of Aflibercept Educational Materials (Annex 5, Table 4; Question 23)

Prior to the study, Bayer widely distributed educational materials to potential aflibercept prescribers across all countries. In general, the educational materials included the aflibercept prescriber guide, injection procedure video, patient booklet, audio CD, and SmPC. Physicians participating in the study were asked to indicate whether or not they received and reviewed aflibercept educational materials (Table 6).

The majority of physicians (87%) reported receiving the summary of product characteristics (SmPC); of those, 89% reviewed it. The proportions of reported receipt and review were similar across countries.

Most physicians (77%) reported receiving the prescriber guide; of those, 86% reviewed it. However, reported receipt of prescriber guide varied across countries with Italy and Spain reporting lower receipt (72% and 64%, respectively) compared with other countries (82-95%). Among those who received the prescriber guide, review of the guide was consistently high across countries.

Half of physicians (50%) reported receiving the intravitreal injection procedure video; of those, 67% reviewed it. The proportion of receipt varied among the five countries, ranging from 36% in Spain to 57% in France.

Finally, 54% reported receiving the patient booklet, including a patient information audio and patient information leaflet; of those, 69% of physicians reviewed it. The proportion of receipt of the patient booklet

varied dramatically; from a high of 74% in the UK to a low of 30% in Spain. The proportion of physicians that reviewed the patient booklet among those who received it was lowest in Germany (50%) and ranged from 65% to 81% in the other countries.

Table 6. Receipt and Review of Materials

Question	Number of Physicians (%)					
	France n = 69	Germany n = 59	Italy n = 99	Spain n = 102	UK n = 99	Overall N = 428
Summary of Product Characteristics						
Received	62 (90)	56 (95)	82 (83)	82 (80)	91 (92)	373 (87)
Reviewed (among those who received it)	50 (81)	49 (88)	77 (94)	71 (87)	84 (92)	331 (89)
Eylea Prescriber Guide						
Received	57 (83)	56 (95)	71 (72)	65 (64)	81 (82)	330 (77)
Reviewed (among those who received it)	47 (82)	45 (80)	65 (92)	57 (88)	70 (86)	284 (86)
Intravitreal injection procedure video						
Received	39 (57)	33 (56)	50 (51)	37 (36)	53 (54)	212 (50)
Reviewed (among those who received it)	20 (51)	20 (61)	38 (76)	30 (81)	35 (66)	143 (67)
Patient Booklet including a Patient Information Audio CD and the Patient Information Leaflet						
Received	43 (62)	38 (64)	45 (45)	31 (30)	73 (74)	230 (54)
Reviewed (among those who received it)	28 (65)	19 (50)	34 (76)	25 (81)	52 (71)	158 (69)

Note: A stratification variable was derived based on responses to question 23 (“Have you received the material?” and “Have you reviewed the material?”). The categories for this stratification are 1) “reviewed,” 2) “received, but did not review,” and 3) “did not receive.” Table 3 presents the results for this stratification variable.

Table 6 presents the proportion of physicians who responded “Yes” to “Have you received the material?” and “Yes” to “Have you reviewed the material?” directly as asked in question 23.

10.1.4.3 Physician Ratings of Aflibercept Education Materials (Annex 5, Table 5; Question 24)

Physicians were asked to rate the materials that they had previously indicated receiving on a scale from 1 (not at all helpful) to 4 (extremely helpful).

Among physicians who reported receiving each item, ratings of 3 or 4 were given to the SmPC by 77% of physicians; to the prescriber guide by 76% of physicians, to the intravitreal injection procedure video by 62% of physicians, to the patient booklet by 75% of physicians, to the patient information audio CD by 63% of physicians, and to the patient information leaflet by 78% of physicians.

Within each country the majority of physicians who received each of the materials rated that material as 3 or 4 with the exception of in France, where 61% of physicians rated the intravitreal injection procedure video with 1 (not at all helpful) or 2, and in Spain, where 40% of the physicians rated the patient information audio CD with 1 or 2.

10.1.4.4 Physician Use of Patient Booklet (Annex 5, Table 6; Question 26-27)

Physicians were asked, "considering the patients under your care who are receiving Eylea injections, to how many did you provide a Patient Booklet?" The overall distribution among physicians was almost evenly divided between the response categories "all of my patients," "most of my patients," "a few of my patients," and "none of my patients." Across countries the distribution of responses was variable; with 82% in the UK responding "all" or "most," compared with much lower percentages in the other countries (30-48%).

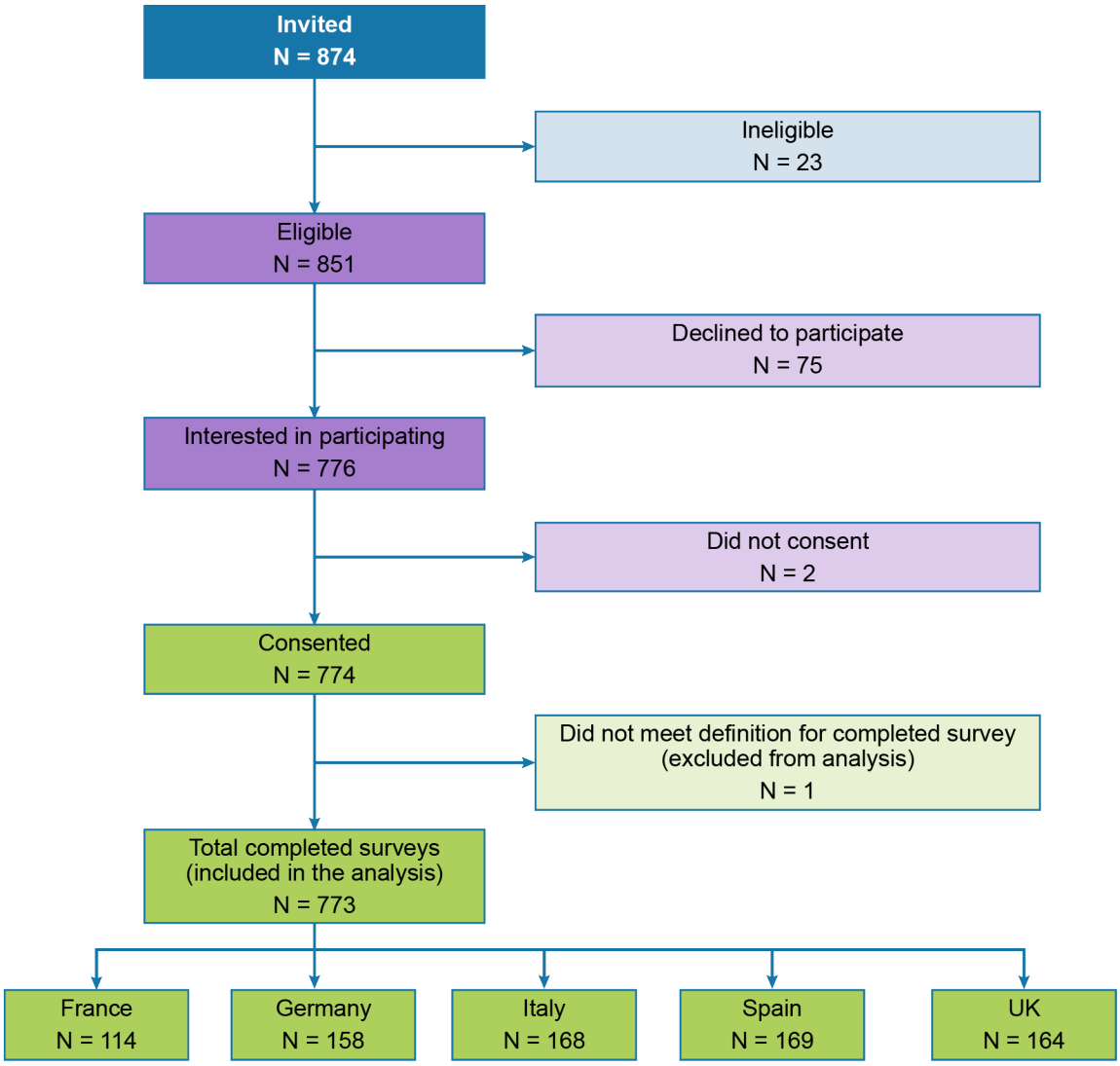
Among physicians who indicated that they provided the patient booklet to their patients, overall and within each country, greater than 90% responded that they provide it "before the start of treatment with Eylea."

10.2 Patient Assessment Results

10.2.1 Participants

Across the 46 sites, 874 patients were approached about participation in the study; of these, 23 were deemed ineligible based on the screening criteria. Of the 851 patients who were eligible, 75 declined to participate and 2 did not consent, leaving 774 patients who were interested in completing the questionnaire and consented. One patient did not meet the criteria for a completed questionnaire; this patient was not included in the final analysis data set. Therefore, 773 patients (88% of those invited and eligible) were included in the final analysis data set. Patient counts ranged from 1 to 30 across the 46 sites, with an average of 16.8 per site. The overall response rate was 91%. Figure 16 provides the disposition of patients invited to participate in the patient assessment.

Figure 16. Disposition of Patients Invited to Participate



10.2.2 Descriptive Data

10.2.2.1 Characteristics of Recruiting Physicians

All physicians (100%) recruited to participate as sites for the patient assessment were retina specialists. Other areas of focus within ophthalmology were less commonly reported: ophthalmology (28%), glaucoma (15%), and cataract (30%). Physicians' experience was measured by years treating patients and was categorised into 5-year increments up to 25 years. Most physicians (91%) had been treating patients for more than 5 years, with durations fairly evenly distributed across the increments beyond 5 years. Nearly a quarter of physicians (22%) reported having been in practice more than 25 years. Seventy-two percent of recruiting physicians were male.

Table 7 provides additional detail on the characteristics of recruiting physicians.

Table 7. Recruiting Physician and Practice Characteristics

Question		Number of Physicians (%)				
	France n = 6	Germany n = 10	Italy n = 10	Spain n = 9	UK n = 11	Overall N = 46
Focus within ophthalmology[a]						
Retina	6 (100)	10 (100)	10 (100)	9 (100)	11 (100)	46 (100)
General ophthalmology	2 (33)	7 (70)	2 (20)	1 (11)	1 (9)	13 (28)
Glaucoma	0 (0)	6 (60)	1 (10)	0 (0)	0 (0)	7 (15)
Cataract	1 (17)	7 (70)	4 (40)	0 (0)	2 (18)	14 (30)
Other	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	2 (4)
Years treating patients						
5 years or fewer	0 (0)	3 (30)	0 (0)	1 (11)	0 (0)	4 (9)
6 to 10 years	2 (33)	1 (10)	4 (40)	0 (0)	1 (9)	8 (17)
11 to 15 years	1 (17)	1 (10)	2 (20)	2 (22)	1 (9)	7 (15)
16 to 20 years	1 (17)	0 (0)	1 (10)	3 (33)	6 (55)	11 (24)
21 to 25 years	1 (17)	0 (0)	1 (10)	2 (22)	2 (18)	6 (13)
More than 25 years	1 (17)	5 (50)	2 (20)	1 (11)	1 (9)	10 (22)
Sex						
Male	3 (50)	9 (90)	7 (70)	7 (78)	7 (64)	33 (72)
Female	3 (50)	1 (10)	3 (30)	2 (22)	4 (36)	13 (28)

[a] This was a “tick all that apply” question; thus, the sum of responses can be greater than 100.

UK = United Kingdom.

10.2.2.2 Patient Demographics (Annex 7, Table 1; Questions 10-11)

Overall, most patients (81%) were aged 66 years or older. Patients were fairly evenly split between males (46%) and females (54%)[3]. Most patients (82%) reported having no university level education. Of the remainder of patients, 17% reported having an undergraduate and/or postgraduate university education, and 1% did not provide an answer.

Table 8 shows responses to these questions by country.

[3] Information on sex was provided by the site on the patient screener recruitment form.

Table 8. Patient Demographics

Question	Number of Patients (%)					
	France n = 114	Germany n = 158	Italy n = 168	Spain n = 169	UK n = 164	Overall N = 773
Age						
18-45 years	0 (0)	2 (2)	1 (1)	2 (2)	2 (1)	7 (1)
46-65 years	20 (18)	31 (19)	26 (16)	38 (23)	26 (16)	141 (18)
66-85 years	79 (69)	107 (67)	125 (74)	109 (65)	115 (70)	535 (69)
86 years or older	15 (13)	18 (11)	16 (10)	20 (12)	21 (13)	90 (12)
Sex						
Female	69 (61)	85 (54)	86 (51)	86 (51)	91 (55)	417 (54)
Male	45 (39)	73 (46)	82 (49)	83 (49)	73 (45)	356 (46)
Education						
No university (primary school, secondary school, university, or professional preparation)	81 (71)	121 (77)	150 (89)	141 (83)	138 (84)	631 (82)
Undergraduate and/or post-graduate university	33 (29)	33 (21)	18 (11)	24 (14)	25 (15)	133 (17)
No answer	0 (0)	4 (3)	0 (0)	4 (2)	1 (1)	9 (1)

UK = United Kingdom.

Note: For patients with multiple responses for Question 11, only the highest indicated education level was used in this analysis.

10.2.2.3 Treatment Characteristics

Per the study inclusion criteria, all patients had been administered aflibercept at least once within the last 6 months. Sites were asked to complete a brief set of questions about each eligible patient's disease and medication history. The information is summarised below. The most common indication for which aflibercept was prescribed was wAMD (71%) followed by DME (19%). Aflibercept was indicated for CRVO and BRVO in 9% of patients, and 2% of patients were prescribed aflibercept for an indication not specified. Over half of patients (60%) had received their first injection of aflibercept within the last year. Most patients (74%) had received one to six aflibercept injections in the past 12 months; the remaining 26% had received more than six aflibercept injections in the past 12 months.

Table 9 provides this information by country.

Table 9. Treatment Characteristics

Question	Number of Patients (%)					
	France n = 114	Germany n = 158	Italy n = 168	Spain n = 169	UK n = 164	Overall N = 773
Indication						
wAMD	84 (74)	95 (60)	136 (81)	116 (69)	118 (72)	549 (71)
DME	19 (17)	34 (22)	25 (15)	35 (21)	31 (19)	144 (19)
CRVO	5 (4)	11 (7)	6 (4)	7 (4)	13 (8)	42 (5)
BRVO	6 (5)	12 (8)	1 (1)	8 (5)	3 (2)	30 (4)
Other	3 (3)	7 (4)	0 (0)	5 (3)	3 (2)	18 (2)
Time since first aflibercept injection						
Less than 1 month	4 (4)	14 (9)	38 (23)	7 (4)	10 (6)	73 (9)
From 1 to 6 months	25 (22)	38 (24)	40 (24)	47 (28)	54 (33)	204 (26)
More than 6 months but less than 1 year	35 (31)	40 (25)	32 (19)	57 (34)	27 (16)	191 (25)
One year or more	49 (43)	65 (41)	58 (35)	58 (34)	72 (44)	302 (39)
No answer	1 (1)	1 (1)	0 (0)	0 (0)	1 (1)	3 (0)
Number of aflibercept injections in the past 12 months						
1-2	12 (11)	24 (15)	73 (43)	54 (32)	30 (18)	193 (25)
3-4	29 (25)	32 (20)	46 (27)	48 (28)	46 (28)	201 (26)
5-6	41 (36)	36 (23)	32 (19)	38 (22)	34 (21)	181 (23)
>6	32 (28)	66 (42)	17 (10)	29 (17)	54 (33)	198 (26)

BRVO = branch retinal vein occlusion; CRVO = central retinal vein occlusion; DME = diabetic macular oedema; UK = United Kingdom; wAMD = wet age-related macular degeneration.

10.2.2.4 Assistance with Materials and Treatment Decisions (Annex 7, Table 1, Question 12)

Given the age of the patient population studied, 3 questions were included in the patient survey to estimate the level of help patients receive from anyone other than their doctor or nurse (e.g., family member, friend, or caregiver) in relation to their eye treatment (Table 10). Specifically, patients were asked to indicate how often (i.e., none of the time, some of the time, most of the time, or all of the time) they need someone other than their doctor or nurse to read information materials to them, explain information materials to them, and make treatment decisions for them.

Two-thirds of patients indicated that they do not need someone to help them with reading information materials (66%) or explaining materials to them (66%). Nearly a quarter of patients reported that some or most of the

time they have someone other than their doctor or nurse read information materials (22%) or explain materials to them (25%), and the remaining patients reported having assistance all of the time with someone reading materials (10%) or having materials explained to them (8%).

Most patients (79%) reported that they make treatment decisions on their own; 16% receive help with treatment decisions some or most of the time; and only 4% reported receiving assistance with treatment decisions all of the time.

Table 10. Assistance With Materials and Treatment Decisions

Question	Number of Patients (%)					
	France n = 114	Germany n = 158	Italy n = 168	Spain n = 169	UK n = 164	Overall N = 773
How often do you need to have someone other than your doctor or nurse READ information materials to you?						
None of the time	84 (74)	116 (73)	103 (61)	96 (57)	115 (70)	514 (66)
Some of the time	12 (11)	23 (15)	36 (21)	23 (14)	26 (16)	120 (16)
Most of the time	6 (5)	5 (3)	12 (7)	18 (11)	10 (6)	51 (7)
All of the time	10 (9)	8 (5)	17 (10)	28 (17)	11 (7)	74 (10)
I don't know	2 (2)	6 (4)	0 (0)	4 (2)	2 (1)	14 (2)
How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you?						
None of the time	87 (76)	109 (69)	107 (64)	91 (54)	118 (72)	512 (66)
Some of the time	14 (12)	34 (22)	36 (21)	35 (21)	31 (19)	150 (19)
Most of the time	8 (7)	3 (2)	10 (6)	14 (8)	6 (4)	41 (5)
All of the time	4 (4)	6 (4)	15 (9)	25 (15)	8 (5)	58 (8)
I don't know	1 (1)	6 (4)	0 (0)	4 (2)	1 (1)	12 (2)
How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you?						
None of the time	91 (80)	127 (80)	121 (72)	125 (74)	144 (88)	608 (79)
Some of the time	11 (10)	18 (11)	30 (18)	21 (12)	14 (9)	94 (12)
Most of the time	6 (5)	3 (2)	7 (4)	9 (5)	4 (2)	29 (4)
All of the time	5 (4)	4 (3)	10 (6)	12 (7)	1 (1)	32 (4)
I don't know	1 (1)	6 (4)	0 (0)	2 (1)	1 (1)	10 (1)

10.2.3 Outcome Data

Not applicable.

10.2.4 Main Results

In the following sections, we present key results from the patient survey. The results are organised in the following categories: (1) knowledge of key safety information and (2) patient preinjection instructions and receipt and use of aflibercept educational materials.

First, we describe the results for the overall sample, then results stratified by country and patient experience with the aflibercept patient booklet.

Annex 7 includes tables presenting the complete set of knowledge question results for patients overall and by country. Annex 8 includes tables presenting results by other stratification variables. These results are broken into those stratified by Patient Booklet and those stratified by "How often do you need to have someone other than your doctor or nurse:

READ information materials to you,"

EXPLAIN information materials to you," and

MAKE TREATEMENT DECISION for you."

10.2.4.1 Knowledge of Key Safety Information

Health Conditions to Discuss with Doctor Prior to Injection

In a series of nine questions related to issues and health conditions, patients were asked whether or not they should tell their ophthalmologist about them before having an aflibercept injection (Figure 17 through Figure 19). The majority of patients correctly responded to almost all of the questions regarding issues and health conditions (ranging from 85% to 92% on individual items) with the exception of a question related to pregnancy and breastfeeding for which correct responses were lower (52%).

On average, patients' knowledge of these items was slightly higher in Germany and lower in France (Annex 7, Table 2, Question 1). Knowledge was fairly consistent across groups that read the patient booklet, for those who received but did not read it, and for those who did not receive it (Annex 8, Table 2a, Question 1). Likewise, knowledge did not differ noticeably based on the level of help patients received with reading and explaining materials and making treatment decisions (Annex 8, Tables 2b, 2c, and 2d, Question 1).

Figure 17. Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Question 1a, 1b, 1c) (N = 773)

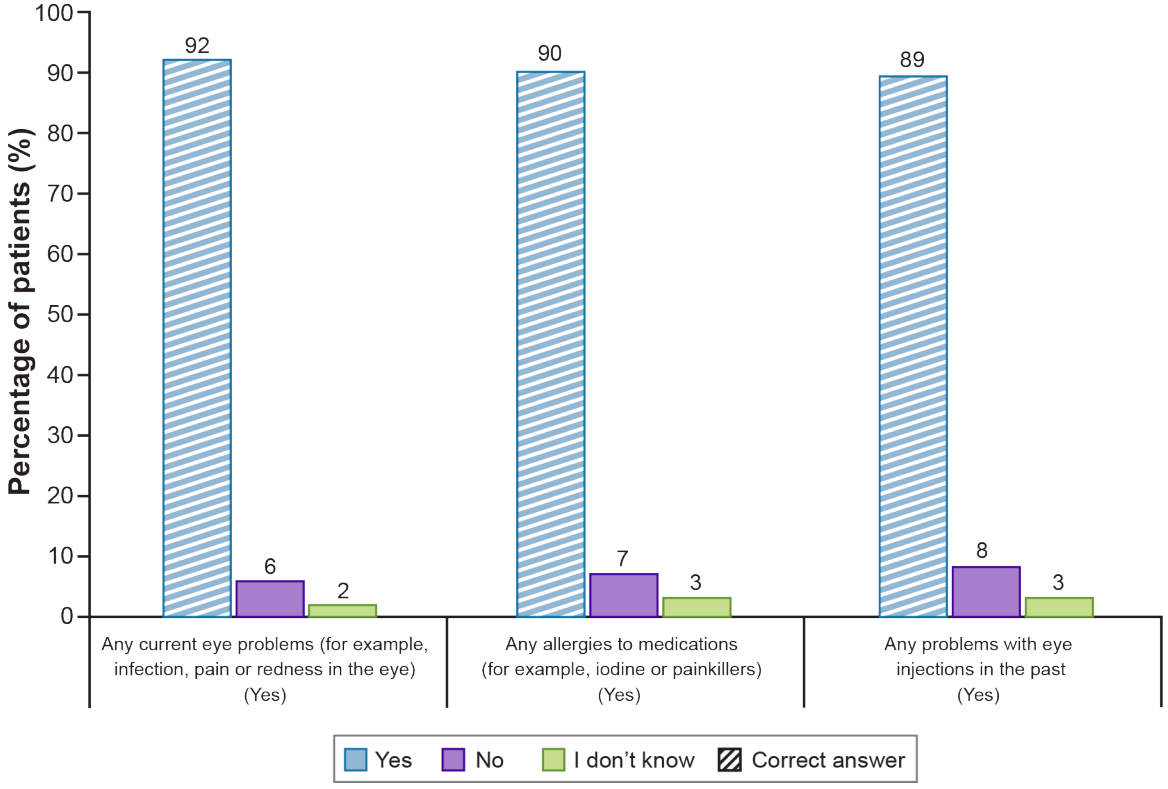


Figure 18. Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Question 1d, 1e, 1f) (N = 773)

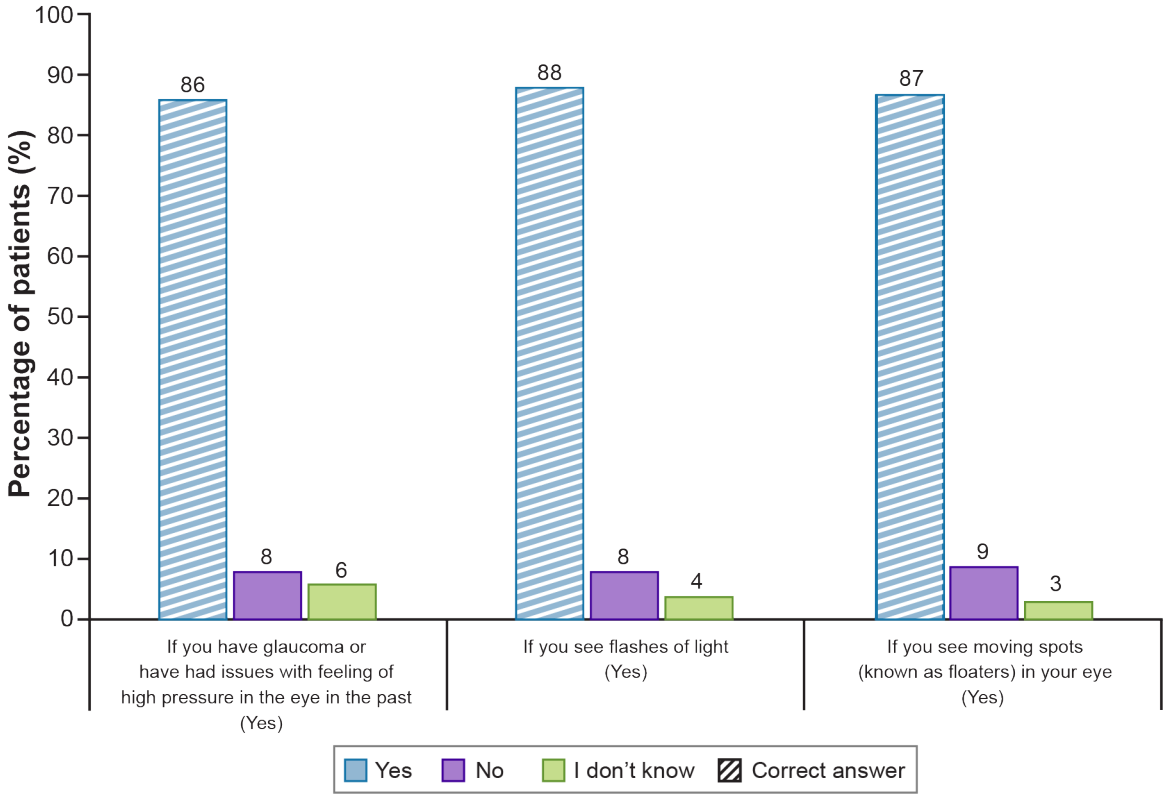
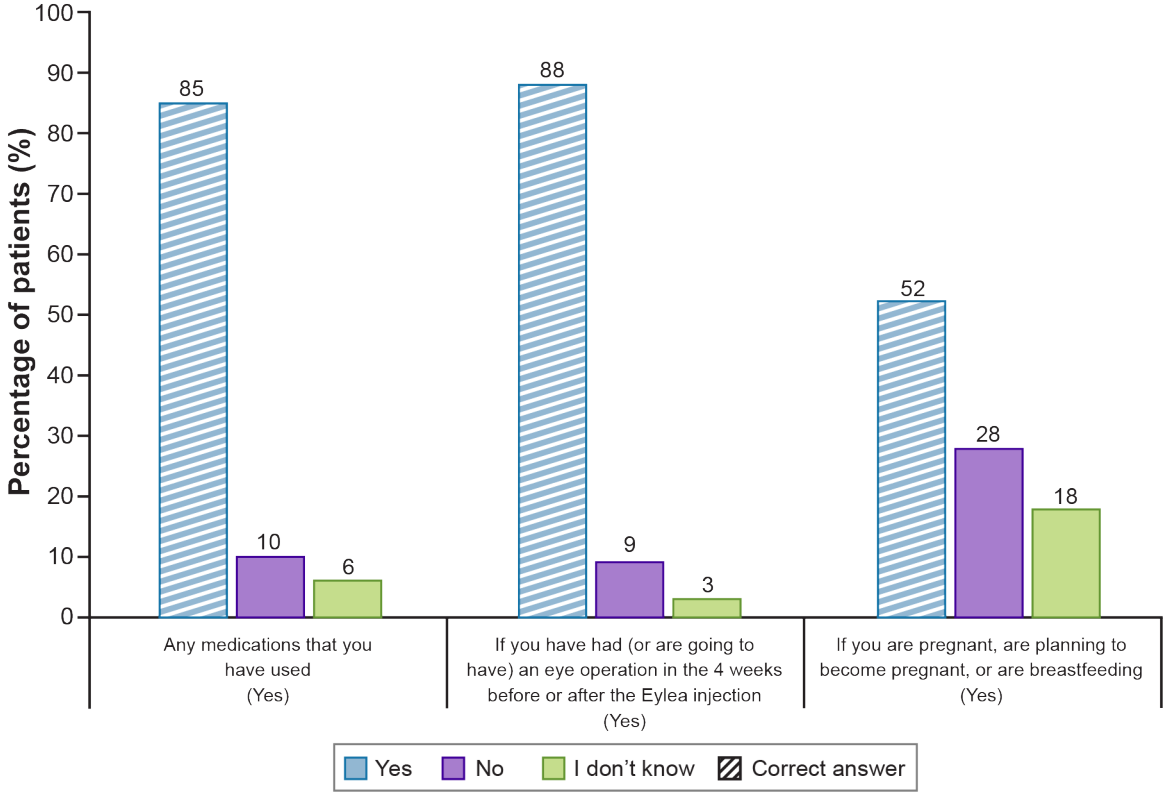


Figure 19. Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Question 1g, 1h, 1i) (N = 773)



Possible Side Effects

Patients' knowledge of the possible side effects with aflibercept varied by side effect (Figure 20 through Figure 22). Knowledge was higher for "eye pain" (74% reported correctly), "cloudy or blurred vision" (73%), "red or bloodshot eye" (70%), "sudden appearance or increase in moving spots" (68%), "sensitivity to light" (67%), and "eye infection" (61%). Knowledge was lower for "seeing halos around lights" (57% reported correctly), "sudden flashes of light" (53%), and "detachment of the gel-like substance inside the eye from the retina" (42%).

Overall, patients in Italy demonstrated a slightly better knowledge of side effects than other countries, and patients in France showed correct knowledge proportions that were lower than other countries (Annex 7, Table 3, Question 2). On average, knowledge was higher for those patients who read the patient booklet (Annex 8, Table 3a, Question 2). Likewise, knowledge did not differ noticeably based on the level of help patients received with reading and explaining materials and making treatment decisions (Annex 8, Tables 3b, 3c, and 3d, Question 2).

Figure 20. We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] a possible side effect of Eylea? (Question 2a, 2b, 2c, 2d) (N = 773)

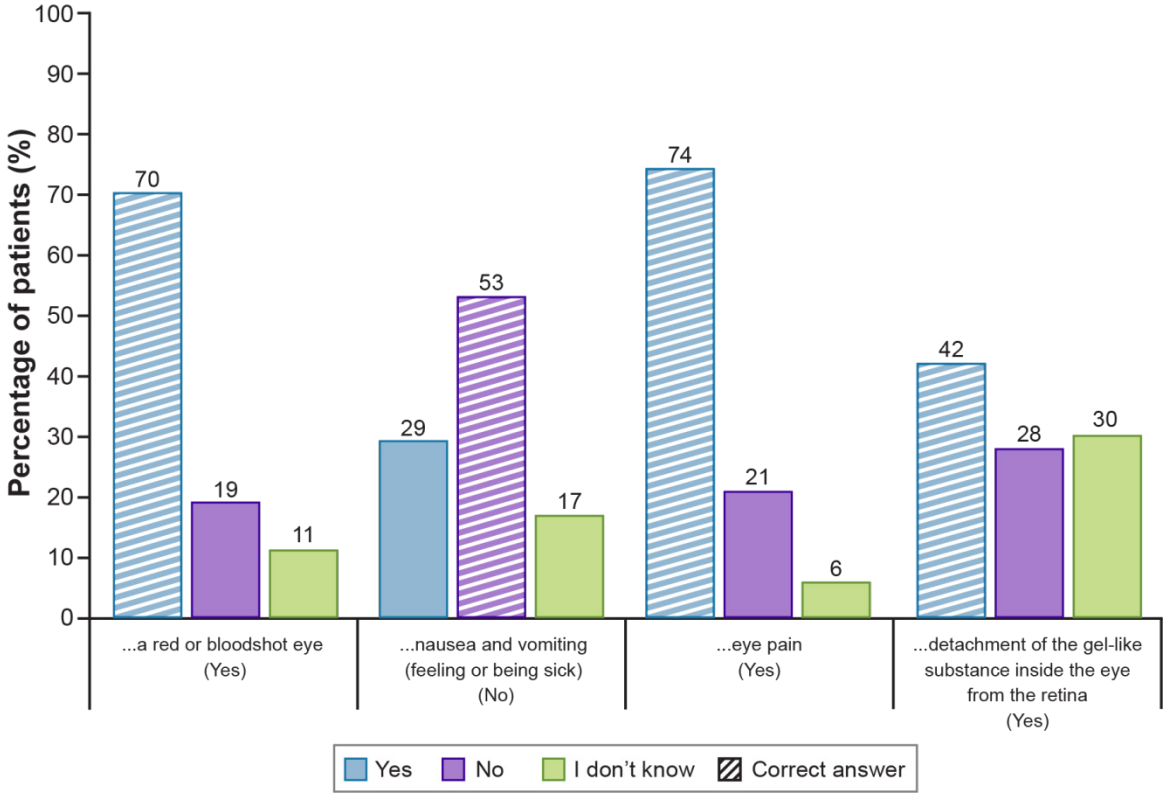


Figure 21. We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] a possible side effect of Eylea? (Question 2e, 2f, 2g) (N = 773)

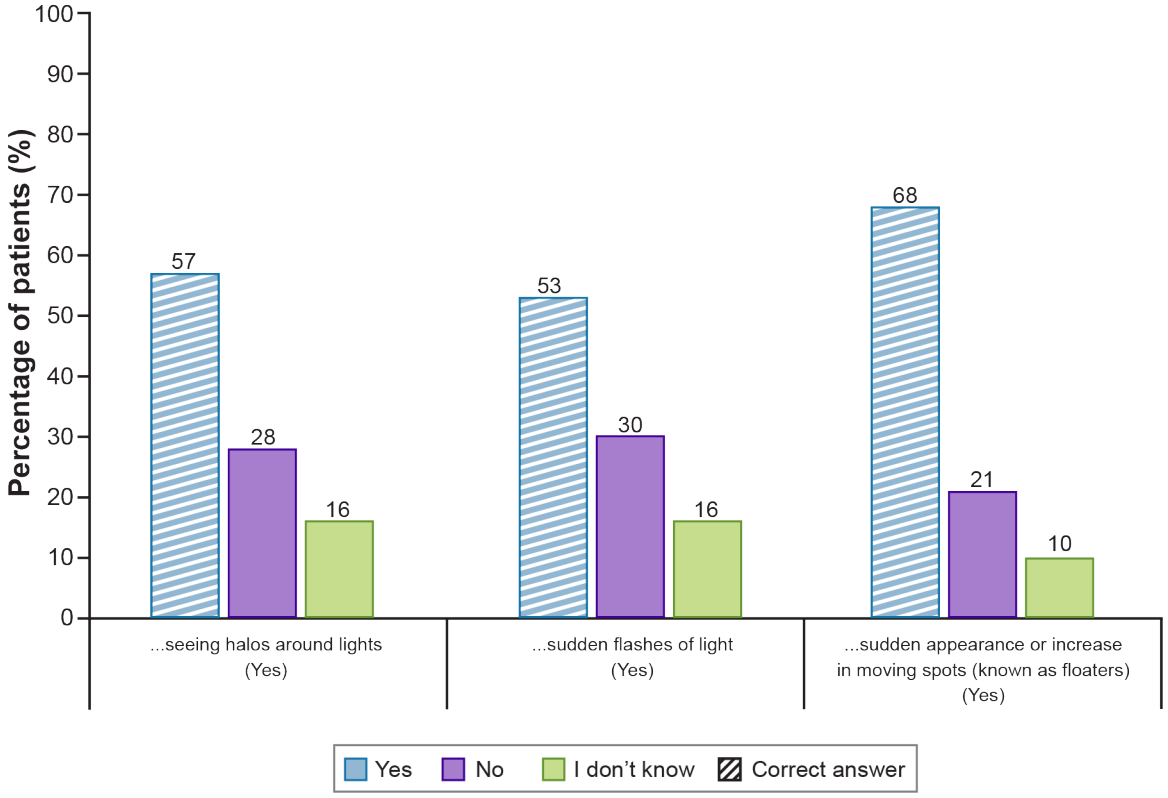
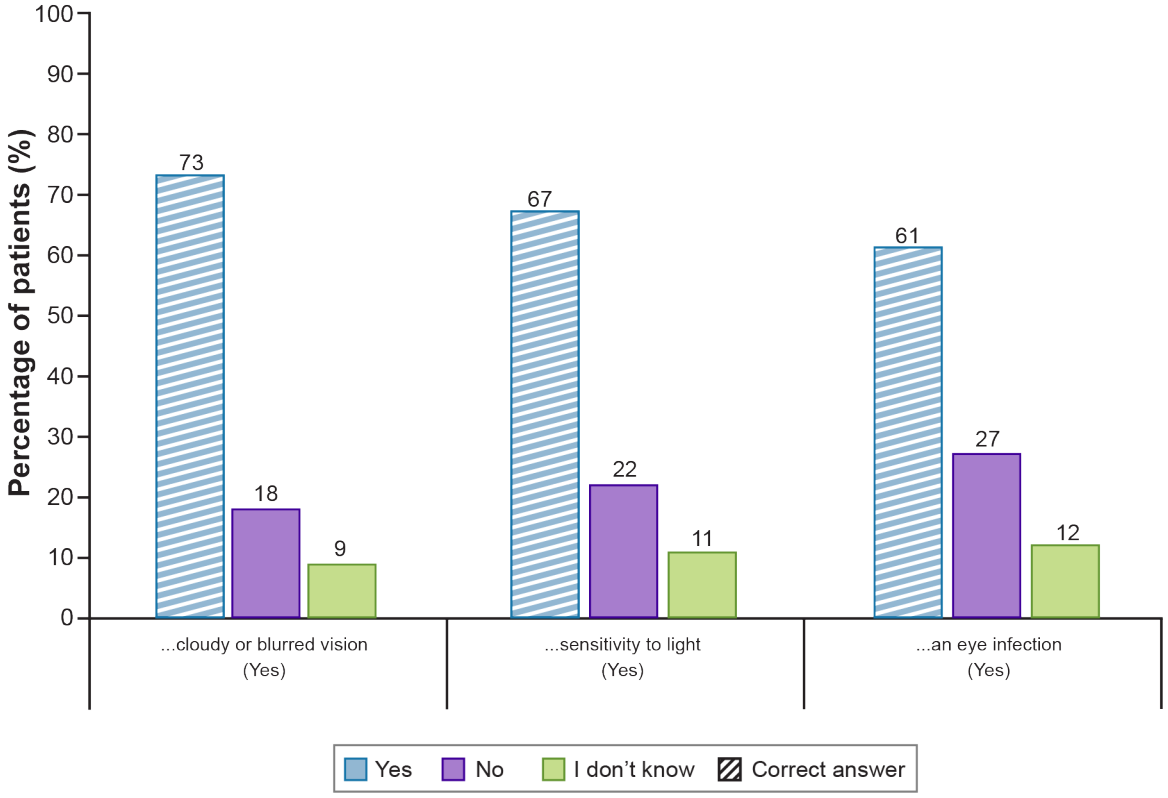


Figure 22. We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] a possible side effect of Eylea? (Question 2h, 2i, 2j) (N = 773)

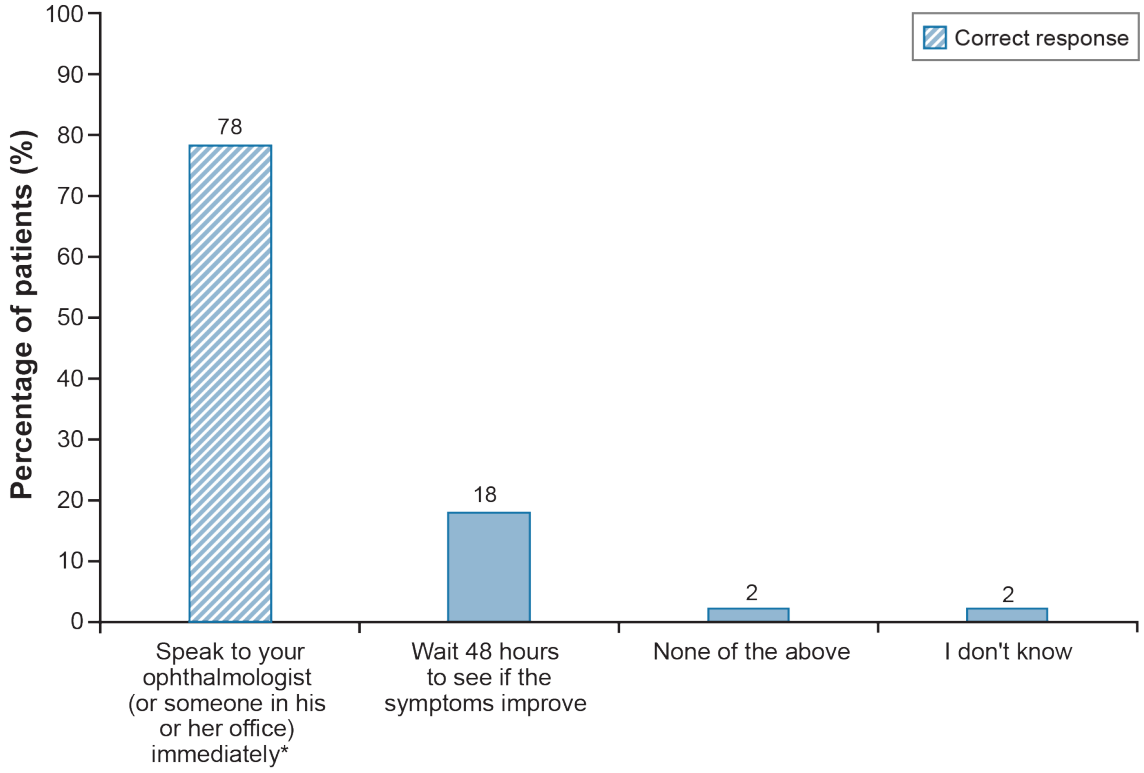


Appropriate Action in Response to Side Effects

Overall, patients' knowledge of what to do if they think they might be having a side effect from aflibercept was high (Figure 23). Most patients (78%) knew that they should speak to their ophthalmologist (or someone in his or office) immediately. Knowledge was highest in Italy (92% correct) and lowest in France (68%) and the UK (67%) (Annex 7, Table 4, Question 3).

The proportion of correct responses was slightly higher for patients who read the patient booklet (87%) and lowest for those patients who did not receive it (74%) (Annex 8, Table 4a, Question 3). In general, knowledge was similar across patients despite receiving different levels of help with reading and explaining educational materials and with making treatment decisions (Annex 8, Tables 4b, 4c, and 4d, Question 3). The exception was with patients who reported that they need help "all of the time." Their knowledge was a little lower.

Figure 23. What should you do if you think you might be having a side effect from your Eylea injection? (Question 3) (N = 773)



10.2.4.2 Patient Preinjection Instructions and Receipt and Use of Aflibercept Educational Materials (Annex 7, Tables 5 & 6, Questions 4-9)

Most patients (71%) reported that before their first injection of aflibercept, their ophthalmologist (or someone in his or her office) told them what to expect during and after the injection. This proportion ranged from 65% in Germany to 80% in Italy.

Thirty-eight percent of patients (ranging from a low of 4% in France to a high of 61% in Italy) reported that they received the Eylea Patient Booklet. Of those, 86% reported that they reviewed it. There was considerable variability in the proportion of patients who had reviewed it by country; however, sample sizes are very small.

Twenty-three percent of patients (ranging from a low of 1% in France to a high of 40% in Italy) reported that they received the aflibercept audio CD. Of those, 39% reported that they reviewed it. There was some variability in the proportion that reviewed by country, but sample sizes are small.

Thirty-five percent of patients (ranging from a low of 12% in Spain to a high of 67% in Italy) reported that they received the Eylea Patient Information Leaflet. Of those, 77% reported that they reviewed it. There were only minor differences in the proportion of patients who reviewed by country.

A small proportion of patients (10%) indicated that their ophthalmologist (or someone in his or her office) gave them additional information materials about aflibercept beyond those specified in the questionnaire. In France, Italy, Spain, and the UK, these materials included an informed consent form.

Patients were asked to indicate which aflibercept information material was most useful. Half of patients (50%) indicated that the patient booklet was most useful, followed by a quarter of patients (23%) who indicated that the patient information leaflet was most useful. Responses varied somewhat by country.

A small number of patients reported that they did not read or listen to any of the aflibercept information materials and were asked to indicate their reasons. The most commonly cited reasons for why patients did not read the materials were "I don't know, I don't remember" (21%), "due to problems with [their] vision" (18%), "someone else explained the information to [them]" (16%), and "other" (23%).

Table 11 provides information on receipt and review of materials by country.

Table 11. Receipt and Review of Materials

Question	Number of Patients (%)					
	France n = 114	Germany n = 158	Italy n = 168	Spain n = 169	UK n = 164	Overall N = 773
Patient Booklet, "Your Guide to Eylea"						
Received	4 (4)	81 (51)	103 (61)	31 (18)	72 (44)	291 (38)
Reviewed (among those who received it)	4 (100)	65 (80)	98 (95)	18 (58)	64 (89)	249 (86)
Audio CD						
Received	1 (1)	32 (20)	67 (40)	23 (14)	54 (33)	177 (23)
Reviewed (among those who received it)	1 (100)	10 (31)	31 (46)	11 (48)	16 (30)	69 (39)
Patient Information Leaflet						
Received	30 (26)	37 (23)	113 (67)	21 (12)	68 (41)	269 (35)
Reviewed (among those who received it)	24 (80)	25 (68)	89 (79)	13 (62)	56 (82)	207 (77)

10.3 Other Analyses

10.3.1 Comparison of Recruiting and Non-recruiting Physicians

Two independent groups of physicians were selected to participate in the patient and physician assessments: 46 physicians (between 6 and 11 from each country) who recruited patients for the patient assessment (*recruiting physicians*) and 428 physicians who only participated in the physician assessment (*non-recruiting physicians*). Both groups were asked to complete the same physician questionnaire. Analyses were conducted to compare responses between recruiting and non-recruiting physicians to explore whether preparing the recruiting physicians to enrol patients into the study created greater awareness of the safety information.

Annex 9 presents the complete set of tables providing the questionnaire responses from the recruiting physicians.

10.3.1.1 Physician and Practice Characteristics

About 75% of both the recruiting and non-recruiting physicians were males. Recruiting physicians tended to have more years of treating patients, with approximately 60% reporting 16 or more years, compared to about 40% among the non-recruiting physicians. Compared with non-recruiting physicians, recruiting physicians were more likely to describe their focus within ophthalmology as retina (100% vs. 74%), and less likely to describe it as general ophthalmology (28% vs. 54%), glaucoma (15% vs. 35%), or cataract (30% vs. 45%)[4].

10.3.1.2 Knowledge

The recruiting physicians did better on every single knowledge question, often only slightly higher, but in some instances quite markedly. The two groups performed most similarly on the questions related to side effects and on injection procedures, as well as the questions on safe use, with the exception that recruiting physicians showed better knowledge of the fact that women of childbearing potential must use effective contraception during treatment and for at least 3 months after the last aflibercept injection (78% vs. 48%).

10.3.1.3 Sources of Information About Aflibercept

For every potential source listed, the recruiting physicians were more likely to report receiving information about aflibercept (e.g. SmPC 93% vs. 87%, Prescriber Guide 87% vs. 77%; Injection Procedure Video 65% vs. 50%; Patient Booklet including a Patient Information Audio CD and the Patient Information Leaflet 80% vs. 54%). Among those reporting receiving each specific material, a higher proportion of the recruiting physicians reported that they reviewed the material. Among the recruiting and non-recruiting physicians using each source, both types of physicians rated the helpfulness of most of the sources similarly on a scale of 1 (not at all helpful) to 4 (extremely helpful). The intravitreal injection procedure video received somewhat less positive ratings among the recruiting physicians than among the non-recruiting physicians (7% vs. 29% extremely helpful).

10.3.1.4 Physician Experience With Information Materials

Among both the recruiting physicians and the non-recruiting physicians, about 50% reported that they provide the Patient Booklet to either all or most of their patients who receive aflibercept.

10.3.2 Comparison of Patient Knowledge Stratified by Recruiting Physician Knowledge

We explored whether there was an association between the proportion of correct responses among the recruiting physicians and the proportion of correct responses among the patients recruited at their sites. To do this, we created an overall knowledge score for each recruiting physician by calculating the percentage of correct responses selected out of all correct responses in the questionnaire. We then created three groups of physicians selecting cut points in their percentage of correct responses to make 3 categories of physicians of approximately similar sizes and called them "highest knowledge tertile," "middle knowledge tertile," and "lowest knowledge tertile." We then stratified the patient data by their recruiting physician's knowledge category. Overall, of the 773 patients recruited at sites, 245 were from a site with a physician in the highest knowledge tertile, 255 were from a site with a physician in the middle knowledge tertile, and 273 were from a site with a physician in the lowest knowledge tertile.

Examining the stratified patient results, we found the distribution of correct responses on the knowledge questions was slightly higher in the patients whose physician was in the highest knowledge tertile. More patients of physicians in the highest knowledge tertile correctly answered all nine questions related to the "health conditions to discuss with physician prior to injection" compared with either of the other tertiles (50%

[4] This was a "tick all that apply" question; thus, the sum of responses can be greater than 100.

vs. 35% patients of physicians in middle tertile and 32% patients of physicians in lowest tertile). Similarly, on the 10 questions about side effects, patients from the physicians in the highest knowledge tertile did the best; 50% correctly answered at least 8 questions whereas only 29% of patients of physicians in the middle knowledge tertile and 33% of patients of physicians in the lowest knowledge tertile got at least 8 correct.

Annex 10 presents the tables with patient knowledge questions stratified by physician knowledge tertile.

10.3.3 Comparison of Patient Participants to Non-participants

Each site kept a simple log with information on the number of patients approached about the study, the number of patients confirmed eligible, and the number of patients who refused. For every patient approached about the study and deemed eligible, the site recorded the patient's age range, sex, and the indication for which aflibercept was prescribed.

There were 773 patients who completed the questionnaire and 77 who refused participation. The 77 eligible patients who did not participate provided the following reasons for declining: 49 not interested, 10 too busy, 8 had not received the patient booklet, 1 not feeling well, 3 - other (unspecified), and 6 did not give a reason. Compared to participants, nonparticipants were slightly older (23% vs. 13% > 85 years), more likely to be female (61% vs. 54%), and reported more aflibercept injections in the past 12 months (Table 12). The distribution for indication was similar across the two groups.

Table 12. Comparison of Patient Participants to Nonparticipants

Characteristic	Number of Patients (%)	
	Completed[a] (N = 773)	Declined (N = 77)
Age range		
18-45 years	7 (1)	0 (0)
46-65 years	143 (18)	10 (13)
66-85 years	526 (68)	49 (64)
86 years or older	97 (13)	18 (23)
Sex		
Female	417 (54)	47 (61)
Male	356 (46)	30 (39)
Indication(s) aflibercept prescribed[b]		
wAMD	549 (71)	63 (82)
DME	144 (19)	10 (13)
CRVO	42 (5)	3 (4)
BRVO	30 (4)	1 (1)

Characteristic	Number of Patients (%)	
	Completed[a] (N = 773)	Declined (N = 77)
Other	18 (2)	0 (0)
Number of aflibercept injections in the past 12 months		
1-2	193 (25)	9 (12)
3-4	201 (26)	13 (17)
5-6	181 (23)	14 (18)
>6	198 (26)	28 (36)
No answer	0 (0)	13 (17)

BRVO = branch retinal vein occlusion; CRVO = central retinal vein occlusion; DME = diabetic macular oedema; wAMD = wet age-related macular degeneration.

N/A = not applicable.

[a] Data are based on screening information collected by the sites at recruitment, which may be different than self-reported patient responses to the questionnaire.

[b] This was a “tick all that apply” question; thus, the sum of responses can be greater than 100%.

10.4 Adverse Events/Adverse Reactions

This study was not designed to collect information on individual AEs, serious AEs, or product complaints. However, reports on potential AEs were identified by interviewers during the cognitive pretesting interviews and by site personnel during the interviewer administered patient questionnaire.

Overall, 10 AEs were reported during the study. Six AEs were reported during the cognitive pretest interviews, and four were reported during the course of the main study (Table 13). Those reported during the pretest interviews were related to drugs other than aflibercept and are not described in this report. All 10 AEs were forwarded to Bayer for evaluation; further follow-up, as appropriate, and reporting.

Table 13. Adverse Events Reported During the Full Study

Patient Number	Country	Date of Report	Event Description	Drug
18	France	05-July-16	Headaches	Eylea
002	France	06-July-16	There was a non-serious AE. Pain and bother after the intravitreal injection occurring on the same day. Identical complaint after every injection. Normal upon examination.	Eylea
004	France	09 Aug-16	Subconjunctival haemorrhage/bleeding after intravitreal injection	Eylea
014	France	11-Aug-16	Floating body after injection into left eye	Eylea

AE = adverse event.

11 Discussion

11.1 Key Results

11.1.1 Physicians Assessment

In general, physicians' knowledge of questions related to aflibercept storage and preparation was high; the proportion of correct responses ranged from 74% to 97% for five out of six items on this topic. The remaining item was an inaccurate statement about storing aflibercept at room temperature for up to 48 hours (the actual duration is up to 24 hours). This item was answered correctly by 42% of physicians. Knowledge was also high on questions about injection procedures (83%-96% on individual items).

Physician knowledge on dosing and monitoring varied. Physicians most commonly reported having experience prescribing aflibercept for wAMD, and their knowledge on the dosing requirements was highest for this indication (ranging from 28% on the item related to monitoring to 94% on treatment extension). Physician knowledge of the dosing requirements for BRVO and CRVO, as well as DME was somewhat lower, which may reflect knowledge and/or be a factor of differences in prescribing patterns for these indications. In general, physicians demonstrated a conservative approach to monitoring and responded incorrectly that monitoring is required during the first 12 months. Most physicians (73%) correctly responded that 50 microlitres is the recommended dose for Eylea. Knowledge on questions related to excess volume of aflibercept varied from 67% to 87%.

Overall, physicians' knowledge of actions to prepare patients for treatment with aflibercept was high; correct responses ranged from 63% to 94%. Most physicians (82%) knew the contraindications for aflibercept use, with correct responses to individual items ranging from 85% for active intraocular inflammation to 95% for known hypersensitivity to aflibercept. Fifty-nine percent of physicians reported that aflibercept should not be used in pregnancy unless the potential benefit outweighed the potential risk to the foetus, and an additional 27% of physicians took a more conservative approach and responded that aflibercept should never be used in pregnancy. Half of physicians (48%) selected the correct time frame for which women of childbearing potential must use effective contraception.

Sixty percent of physicians correctly reported that patients' vision should be evaluated immediately after an aflibercept injection by hand movements or counting fingers. Most physicians (79%) knew that an increase in intraocular pressure has been seen within 60 minutes after an aflibercept injection. Knowledge was slightly lower for actions to take in relation to potential increased intraocular pressure (65%-78%). Knowledge was high for recognising signs and symptoms of possible side effects (ranging from 78% to 89% on individual side effects).

In general, physicians' knowledge was consistent across countries with a few exceptions. There were slight variations in knowledge across countries for questions regarding the recommended dose of aflibercept, excess volume, side effects, and how to evaluate a patient's vision immediately after aflibercept injection. In addition, physicians' knowledge regarding whether the vial was reusable between patients was notably lower in Spain where it is common practice for hospitals to use one vial for more than one patient.

Overall, physicians' knowledge did not vary greatly based on their level of experience with the prescriber guide. For most questions, physicians who had reviewed the prescriber guide had slightly higher proportions of correct responses than physicians who received it but did not review it and those who did not receive it.

The majority of physicians (87%) reported that they received the SmPC. Of those, 89% reported that they reviewed the document and 77% found it helpful or extremely helpful. Likewise, most physicians (77%) reported that they received the prescriber guide. Of those, 86% of physicians reviewed the guide and 76% found it to be helpful or extremely helpful. Half of physicians (50%) reported that they received the intravitreal injection procedure video. Of those, 67% of physicians reviewed the video and 62% found it to be helpful or extremely helpful. Similarly, half of physicians (54%) reported that they received the patient booklet. Of those, 69% reviewed the booklet and 75% found it to be helpful or extremely helpful.

The proportions of reported receipt of the SmPC and intravitreal injection procedure video were similar across countries. However, reported receipt of the prescriber guide varied across countries, with Italy and Spain reporting lower receipt (72% and 64%, respectively) compared with other countries (82%-95%). The proportion of receipt of the patient booklet also varied significantly; from a high of 74% in the UK to a low of 30% in Spain.

Overall, half of physicians (50%) reported providing the patient booklet to most or all of their patients (ranging from 30% in Spain to 82% in the UK).

11.1.2 Patient Assessment

Patients' knowledge of the health conditions to discuss with a doctor prior to injection was high (ranging from 85% to 92% on 8 out of 9 individual items). Patient knowledge was lower (52%) on the remaining item related to pregnancy and breastfeeding, likely because this condition is less salient in the aflibercept patient population given the patients' ages (99% of the patients in the study were 46 years or older).

Patient knowledge about possible side effects with aflibercept varied by item, with the highest correct response proportion (74%) for "eye pain" and the lowest (42%) for "detachment of the gel-like substance inside the eye from the retina." Most patients (78%) knew that they should speak to their ophthalmologist (or someone in his or her office) immediately if they think they might be having a side effect from their aflibercept injection.

In general, patients' knowledge was fairly consistent across countries, with slightly higher knowledge on some items in Germany and Italy, and lower knowledge in France. On average, knowledge was higher for those

patients who read the patient booklet. Knowledge did not differ consistently based on the level of help patients received with reading and explaining materials and making treatment decisions.

Thirty-eight percent of patients reported that they received the Eylea Patient Booklet; 23% of patients reported that they received the aflibercept audio CD; and 35% reported that they received the Eylea Patient Information Leaflet. There was considerable variation in the proportions of patients reporting receipt of each item across countries.

11.2 Strengths

A key strength of the study is diversity of physician and patient participants. The targeted numbers of physician (60 to 100 per country) and patient (150 per country) respondents were achieved. The distribution of physicians by their focus within ophthalmology, sex, years treating patients, and aflibercept prescribing practices represented a broad diversity of physicians. The characteristics of patients by demographics and their aflibercept treatment history was diverse, as were the 46 physician practices from which the patients were recruited.

The physician assessment was conducted after physicians had received the educational material and had a chance to use the prescriber guide and the patient booklet in their practice. The patient assessment was conducted after patients had received aflibercept and had the opportunity to receive the educational materials for patients.

Another strength of the patient assessment was the high response rate (773 patients took the questionnaire among 851 who were invited and eligible [91%]) given that the study was introduced by a trusted physician. A relatively small number of patients refused participation (9%), did not consent (< 1%), or did not complete at least one knowledge question on the questionnaire (< 1%). Individuals who declined to participate were slightly older than participants, more likely to be female, and reported more aflibercept injections in the past 12 months.

Accuracy of responses among physicians and patients was facilitated by the pretesting of the questionnaires through formal cognitive pretesting with physicians and patients in each country. The wording of the questions and response choices should have been easily understood by the respondents.

11.3 Limitations

As with all voluntary studies, some limitations are inherent. Although the study was designed to ensure the selection of a diverse and generally representative sample of prescribers and patients to participate in this study, there was no exhaustive list of all aflibercept prescribers and patients from which to draw a sample; hence, it was impossible to select a random sample of all prescribers and patients. Therefore, although participants were diverse in characteristics, the study participants may not necessarily represent all relevant prescribers and patients. In addition, as is true with most surveys, it was possible that respondents who completed the questionnaire differed from non-respondents in characteristics measured in the questionnaire (e.g., knowledge, reading, and use of the educational materials). The direction and magnitude of such potential respondent bias is not known. A comparison of the patient participants and non-participants revealed small differences in age, sex, and number of aflibercept injections in the past 12 months. A comparison of participants and non-participants in the physician assessment was not possible because physicians who did not wish to participate in the survey did not to respond to the invitation and characteristics of the invited physicians were not otherwise available. We could not compare physician and practice characteristics of the physician participants to what is known about the overall prescribing population because that information was not available to us.

Another potential limitation of the patient assessment is that the study could influence sites to provide more education to patients than they normally would provide. To minimise this risk, sites were trained to provide only limited information about the study prior to the patients' participation in the study, and patients were asked to complete the questionnaire at the site prior to receiving any additional counselling about treatment. Site personnel were trained to ensure a thorough understanding of the importance of and processes for conducting an objective interview to mitigate potential biases and an "intervention effect." We also compared the patient responses by knowledge level of the recruiting physicians and found some indication that patients treated by physicians in the highest tertile of knowledge had higher correct response proportions than other patients. The study targeted recruitment of approximately 10 sites per country; however, due to challenges with recruitment, only six sites participated in France. Therefore, patient responses in France reflect the practices of only these six sites.

11.4 Interpretation

Little information is in the public domain to set thresholds for acceptable levels of knowledge and behaviour related to risk minimisation measures. A recent publication (Knox et al., 2015) reported on patient understanding of medication guides from a review of 66 assessment reports submitted to the US Food and Drug Administration. Few of the studies (30%) achieved an 80% knowledge level (% correct) for the single most important risk communicated in the medication guide. The mean knowledge level was 63.8%.

Knowledge and behaviour reflect many factors, including availability and access to information, literacy and numeracy, beliefs, and motivation. Some of the most important information communicated in the aflibercept educational materials is related to side effects. In our study, over 80% of physicians and over 60% of patients responded correctly to the majority of questions on this topic.

Physician knowledge varied across categories of information, with higher knowledge associated with the most important information, including potential side effects and post-instruction procedures for patients. In general, physicians' knowledge of storage and preparation guidelines, safe use, and injection procedures was also high. Knowledge on dosing guidelines varied by indication, which may reflect knowledge and/or be a factor of the recency of indication approval and/or the status of drug reimbursement. In general, physicians demonstrated a conservative approach to the monitoring questions and thus responded incorrectly that monitoring is required during the first 12 months. Physician knowledge was lower on questions related to aflibercept use in pregnancy; however, in several cases, physicians who did not select the correct response chose another response outlining a more conservative approach to treatment.

Patient knowledge was high for health conditions they should tell their ophthalmologist about before having an aflibercept injection. In addition, patient knowledge was high for those side effects that are easier to identify (e.g., "red or bloodshot eye," "eye pain," and "cloudy or blurred vision"). Patient knowledge was lower for side effects that may be more complex to identify (e.g., "detachment of the gel-like substance inside the eye from the retina"). The majority of patients knew that they should speak to their ophthalmologist (or someone else in his or her office) immediately if they think they might be having a side effect, which suggests that they would take appropriate action if there was any question of a side effect.

Little information is in the public domain to be able to compare the percentage of physicians who report receipt of educational materials based on results from postauthorisation safety studies. A recent publication (Brody et al., 2016) reported the results of a multinational survey of 800 European physicians that assessed the receipt of educational materials: for that study, physicians' reported receipt of the educational materials ranged from 16% to 69% across the participating countries.

In our study, the majority of physicians reported receipt of the SmPC (87%) and Eylea Prescriber Guide (77%). A lower proportion of physicians (50%) reported receipt of the Eylea Intravitreal Injection Procedure Video. The video was distributed on a DVD or CD-ROM together with the Prescriber Guide and other materials. Similarly, a lower proportion of physicians (54%) reported receipt of the Patient Booklet.

Patient-reported receipt of the aflibercept educational materials was relatively low with notable variability across countries. Thirty-eight percent of patients reported receipt of the patient booklet, 23% reported receipt of the audio CD, and 35% reported receipt of the patient information leaflet. The relatively low level of reported receipt of materials may reflect poor recall if the materials had indeed been received. While direct comparison cannot be made between physicians and patients in the study because they were two independent samples, in general, there was a disconnect between the proportion of physicians who reported receipt of the patient booklet, the proportion of physicians who reported that they provide the booklet to all or most of their patients, and the proportion of patients who reported receipt of the patient booklet.

Low levels of reported receipt of materials could also reflect various reasons for not receiving the educational material. For example, in some countries (e.g., France and Spain), physicians are required to have patients sign an informed consent form with relevant safety information prior to treatment. Therefore, it is possible that physicians could prioritise competing information sources that are legally required over the patient booklet.

Variability across countries could reflect (1) inherent differences in physician and patient behaviour, (2) variations in prescribing guidelines/practices across country-specific health care systems, (3) differences in distribution practices for educational materials, or (4) different intensity of the educational efforts.

It was encouraging to see that, among physicians and patients who reported receipt of the material, use of the material was high.

11.5 Generalisability

As noted in Section 11.2, the study achieved great diversity in physician and patient characteristics within the five countries, which allowed for stratification of results by those characteristics. We saw heterogeneity of some results by country; it is unknown how well these results would relate to other countries.

12 Other Information

Not applicable

13 Conclusion

The study met its objectives to evaluate whether physicians and their patients receive the educational materials for aflibercept and to assess physician and patient knowledge and understanding of key safety information, as well as the use of the materials. Physicians' reported receipt of the SmPC and prescriber guide was high (87% and 77% respectively). The relatively high level of knowledge among physicians also suggests that the key safety information is available to the treating physicians.

Physicians' knowledge of most important topics was high. For example, knowledge on possible side effects ranged from 78% to 89%. Knowledge varied for topics that are less frequently encountered (e.g., use in women of childbearing potential).

In general, the observed patterns of knowledge among the physicians are as expected—with greatest knowledge on the most important risks emphasised in the educational material and other product information and lower

knowledge on more complex aspects of safe use (e.g., concepts related to dosing and monitoring) for which we would assume that physicians would consult the label and/or prescriber guide rather than relying on recall.

Likewise, levels of patient knowledge were as expected – with highest knowledge on less complex concepts (e.g., health conditions to discuss with a physician and easily identified side effects) and lower knowledge on more complex concepts and issues less salient to the patient population (e.g., more complex side effects and issues pertaining to women of childbearing potential). That fact that patient knowledge was relatively high despite the low reported receipt of the educational materials suggests that patients were receiving the information from other sources. Determining the most effective formats and distribution channels for communicating safe use information to physicians and patients was beyond the scope of this study but remains an important question in risk management.

14 References

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Annex 1. List of Stand-Alone Documents

Number	Document reference number	Date	Title
1		15 May 2017	Full list of principal investigators

Annex 2. List of Ethics Committee Reviews and Approval Dates

INDIVIDUAL ETHICS COMMITTEE APPROVALS

Investigator	Site	EC	Approval Date
Germany			
Prof. Sascha Fauser	Uniklinik Köln Zentrum für Augenheilkunde	Ethikkommission der Universität zu Köln	05.10.2015
Dr. Kai Januschowski	Augenklinik Sulzbach	Ethikkommission der LÄK des Saarlandes	27.10.2015
Laurenz Sonnentag	Universitätsklinikum Schleswig-Holstein Klinik für Augenheilkunde	Ethikkommission der Universität zu Lübeck	16.10.2015
Prof. Karl Heinz Emmerich	Klinikum Darmstadt Klinik für Augenheilkunde	EK der LÄK Hessen	04.11.2015
Dr. Udo Heuer	Medical Eye Care	na	na
Dr. Ben Mehrinfar	Augenklinik am Wittenbergplatz	na	na
Dr. Peter Kaupke	Augenarztpraxis Blankenese, Dr. Kaupke & Partner	na	na
Dr. Tobias Duncker	Augeninstitut Halle Makulazentrum	na	na
Vassilliki Romanou-Papadopoulou	Augenklinik Dardenne	na	na
Dr. Matthias Hartmann	Augenfachärztliche Gemeinschaftspraxis - Dr. Hartmann	na	na
Italy			
Prof. Francesco Semeraro	Spedali Civili di Brescia Divisione Oculistiva Universitaria	Spedali Civili - Brescia Comitato Etico Provinciale Provincia di Brescia	09.11.2016
Dr. Massimo Nicolò	Azienda Ospedaliera IRCCS San Martino IST UO Clinica Oculistica - DINOGMI	Comitato Etico Regionale Liguria - Sezione 2	30.03.2016
Dr. Caterina Musso	Polo Ospedaliero di Rapallo - ASL 4 Chiavarese SC Oculistica	Comitato Etico Regionale Liguria - Sezione 2	30.03.2016
Prof. Claudio Traversi	Ospedale Le Scotte U.O. Oculistica	Comitato Etico Regione Toscana - Area Vasta Sud Est	02.05.2016
Dr. Francesco Ciucci	Ospedale San Pietro Fatebenefratelli Divisione Oculistica	Comitato Etico Lazio I	11.01.2016
Dr. Giuseppe Scarpa	Ospedale Cà Foncello UO Oculistica	Comitato Etico per la Sperimentazione Clinica delle Provincie di Treviso e Belluno	17.12.2015
Dr. Maria Vadalà	Università di Palermo - Dipartimentio di Biomedicina sperimentale e Neuroscienze Cliniche (BIONeC) Sez. Oculistica	Comitato Etico Palermo	16.03.2016

Investigator	Site	EC	Approval Date
Dr. Luca Migliavacca	Ospedale San Paolo UO Oculistica	Comitato Etico Interaziendale Milano Area A	08.06.2016
Dr. Vito Fenicia	Ospedale Sant'Andrea UOC Oculistica	Comitato Etico dell'Universita' "SAPIENZA"	17.03.2016
Dr. Grazia Levi	AO Istituti Ospitalieri SC Oculistica	Comitato Etico d' Area Cremona Mantova Lodi	17.03.2016
Spain			
Dr. Joan Josep Escobar	Hospital Dos Maig	CEIC Consorci Sanitari Integral	27.05.2015
Dr. Pere Romero	Hospital St. Joan Reus	CEIC Hospital Sant Joan Reus	29.10.2015
Dr. Santiago Abengoechea	Clínica Barraquer	CEIC Centro Oftalmología Barraquer	11.11.2015
Dr. Daniel Carrasco Sánchez	General De Jerez	na	na
Dr. Jesus Pareja	Clínica Rementería	na	na
Dr. Manuel Moriche Carretero	Infanta Sofía	na	na
Dr. Ana Chinchurreta	Hospital Costa Del Sol	na	na
Dr. Isabel Pinilla Lozano	Hospital clinico lozano blesa	na	na
Jose Antonio López Garrido	Hospital de Galdakao	CEIC Euskadi	07.01.2016

Annex 3. Physician Questionnaire

EYLEA® (Aflibercept Solution for Injection) Risk Minimisation Program Evaluation

Physician Questionnaire

Introduction and Informed Consent

RTI International, an independent, nonprofit organisation engaging in health and medicine research, is conducting a research study on behalf of Bayer HealthCare (BHC) and would like to invite you to participate. This study is being conducted as part of the ongoing safety and risk management process for Eylea (aflibercept). This is not a marketing survey, but a scientific study conducted at the request of the European Medicines Agency (EMA), the drug regulatory body in the European Union (EU). The purpose of the study is to assess prescribers' understanding of and compliance with the safe use of Eylea.

You have been identified as a potential participant for this evaluation because you are a physician who treats patients who have neovascular (wet) age-related macular degeneration (wAMD), visual impairment due to macular oedema secondary to central or branch retinal vein occlusion (CRVO/BRVO), and/or visual impairment due to diabetic macular oedema (DME). This questionnaire, which takes approximately 20-25 minutes to complete, is being administered to 300 to 500 physicians across several countries within the EU. To confirm your eligibility to participate, please answer the following questions.

S1. Have you prescribed Eylea and/or administered an Eylea injection to a patient in the past 6 months?

Tick <u>all</u> that apply.

- ☐ Prescribed Eylea
- ☐ Administered an Eylea injection
- ☐ Neither of the above **[TERMINATE AND DISPLAY: "It does not appear that you qualify for the survey. Thank you for your time and interest."]**

S2. For which of the following indications have you prescribed and/or administered Eylea in the past 6 months?

Tick <u>all</u> that apply.

- ☐ Neovascular (wet) age-related macular degeneration (wAMD)
- ☐ Visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)

- ☐ Visual impairment due to diabetic macular oedema (DME)
- ☐ Visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)
- ☐ Other indication
- ☐ None of these indications

S3. Which injectable form(s) of Eylea do you use?

Tick all that apply.

- ☐ Prefilled syringe
- ☐ Vial

S4. At your site, who has the primary responsibility for the preparation of an Eylea injection (i.e., opens the vial or pre-filled syringe and prepares the syringe for injection)?

Tick one answer.

- ☐ I am responsible
- ☐ A specialized nurse
- ☐ Pharmacy
- ☐ Laboratory
- ☐ Other

What Will Happen

As a part of this study, you will be asked to complete a 20-25 minute questionnaire related to your general knowledge and understanding about Eylea.

Confidentiality

Any information you provide to us is confidential, and every precaution will be taken to protect your privacy. Your responses will be used only for statistical purposes and will not be disclosed or used in any personally identifiable form for any other purpose, unless otherwise compelled by law. Your responses to this survey (not including your name and contact information) will be shared with RTI researchers in the United States (US) for data analysis and storage purposes. The US has different data protection laws that may not be as strict as in your own country. Your answers will be kept strictly confidential and will not be linked to your name in any report or publication. The risk of participation in this study relates to data security and is minimal, given the strict confidentiality and security procedures in place.

Your willingness to take part in this study will help us ensure that the key safety information about Eylea is being effectively communicated to you and other physicians.

You will be compensated for your participation in this study. Per the code of conduct set by the European Federation of Pharmaceutical Industries and Associations (EFPIA), BHC will post a summary of payments provided to physicians who participated in this study to a public website. No personal identifying physician information will be reported.

[The survey will be programmed online and a link will be provided to a contact page that will include the phone number for Kantar Health for questions related to the study or survey completion and contact information for RTI's Office of Human Research Protection should participants have a question about their rights as a study participant.]

Informed Consent

C1. Please indicate below if you agree to participate in the current study.

- ☐ Yes, I have read the study information provided and agree to participate in this study.
- ☐ No, I do not agree to participate in this study. **[TERMINATE AND DISPLAY: "You have indicated that you do not agree to participate in the study. Thank you for your time."]**

Physician Questionnaire

This questionnaire is designed to gain a better understanding of prescribers' knowledge about the prescribing and administration of Eylea to patients. Additionally, this assessment will be used to determine if the educational materials regarding Eylea, including the Prescriber Guide, are understood accurately and whether these materials could be improved.

The following questions ask about the use of Eylea for the treatment of wAMD, CRVO, BRVO and DME.

[If "prefilled syringe" is the *only* response ticked in S3, SKIP Q1c, Q1e, and Q1g]

[If "vial" is the *only* response ticked in S3, SKIP Q1b, Q1d, and Q1f]

Q1. For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know.

Statement	Yes, this is true	No, this is not true	I don't know
1a. Eylea is a suspension, which contains particulates and is cloudy			
1b. The prefilled syringe of Eylea is for single use only			
1c. The vial of Eylea is reusable between patients and can be used for multiple injections			
1d. The prefilled syringe of Eylea must be stored in the refrigerator (2°C to 8°C)			
1e. The vial of Eylea must be stored in the refrigerator (2°C to 8°C)			
1f. Prior to usage, the prefilled syringe of Eylea may be kept at room temperature for up to 48 hours			
1g. Prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours			
1h. For the intravitreal injection, a 30-gauge x ½ inch injection needle should be used			
1i. Adequate anaesthesia and asepsis (e.g., use of povidone iodine) must be provided for the patient			

The following questions ask about Eylea dosing recommendations and product information

Q2. What is the recommended dose for Eylea?

☐ 12.5 microlitres (0.5 mg)

☐ 50 microlitres (2 mg)

☐ 90 microlitres (3.6 mg)

☐ 100 microlitres (4 mg)

☐ I don't know

[If wAMD is ticked in S2, display Q3; otherwise, skip Q3.]

Q3. For each of the following statements related to the Eylea dosing and monitoring recommendations for the treatment of wAMD, please indicate if the statement is true, not true, or if you do not know.

Dosing recommendations for wAMD	Yes, this is true	No, this is not true	I don't know
During the first 12 months, treatment is initiated with one injection per month for three consecutive doses, followed by one injection every 2 months.			
During the first 12 months, there is no requirement for monitoring between injections.			
After the first 12 months, the treatment interval may be extended based on visual and anatomical outcomes.			
After the first 12 months, the schedule for monitoring should be determined by the treating physician and may be more frequent than the schedule of injections.			

[If CRVO or BRVO is ticked in S2, display Q4; otherwise, skip Q4.]

Q4. For each of the following statements related to the Eylea dosing recommendations for the treatment of macular oedema secondary to CRVO or BRVO, please indicate if the statement is true, not true, or if you do not know.

Dosing recommendations for CRVO and BRVO	Yes, this is true	No, this is not true	I don't know
After the initial injection, treatment is given monthly.			
The interval between two doses should not be shorter than 2 months.			
If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued.			
Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity.			

[If DME is ticked in S2, display Q5; otherwise, skip Q5.]

Q5. For each of the following statements related to the Eylea dosing recommendations for the treatment of DME, please indicate if the statement is true, not true, or if you do not know.

Dosing recommendations for DME	Yes, this is true	No, this is not true	I don't know
Eylea treatment is initiated with one injection per month for five consecutive doses.			
After the first 5 months, Eylea treatment is followed by one injection every 2 months.			
During the first 12 months, there is no requirement for monitoring between injections.			

[If "prefilled syringe" is ticked in S3, display Q6 and Q7; otherwise skip Q6 and Q7]

Q6. The prefilled syringe of Eylea contains excess volume which should be expelled before injecting.

☐ True

☐ False

☐ I don't know

Q7. To eliminate all potential bubbles and to expel excess medicinal product from the prefilled syringe, physicians should slowly depress the plunger to align the cylindrical base of the plunger to which of the following positions:

☐ With the black dosing line on the syringe (equivalent to 50 microlitres)

☐ Below the black dosing line on the syringe

☐ Above the black dosing line on the syringe

☐ I don't know

[If "vial" is ticked in S3, display Q8 and Q9; otherwise skip Q8 and Q9]

Q8. The Eylea vial contains more than the recommended dose of Eylea and excess volume should be expelled before injecting.

☐ True

☐ False

☐ I don't know

Q9. After removing all of the drug from the Eylea vial with a syringe, the plunger of the syringe should be depressed until the tip aligns with the line that marks which number of millilitres (ml) on the syringe?

☐ 0.05 ml

☐ 0.1 ml

☐ 0.15 ml

☐ 0.2 ml

☐ 0.5 ml

☐ I don't know

Q10. What should you do to prepare the patient before the start of treatment with Eylea?

Tick <u>all</u> that apply.

☐ Provide the Patient Booklet which includes a Patient Information Audio CD and Patient Information Leaflet

☐ Explain the implications of anti-VEGF treatment

☐ Inform the patient to report any signs and symptoms potentially associated with serious adverse events and provide information on when to seek medical attention

☐ None of the above

☐ I don't know

Q11. Eylea is contraindicated in which of the following patients?

Tick <u>all</u> that apply.

☐ Patients with a known hypersensitivity to Eylea or to any of the excipients (e.g., non-active ingredients)

☐ Patients with active or suspected ocular or periocular infection

☐ Patients with high blood pressure

☐ Patients with active severe intraocular inflammation

☐ None of the above

☐ I don't know

Q12. What is the recommended use of Eylea in women of childbearing potential?

Tick <u>all</u> that apply.

☐ Women of childbearing potential must use effective contraception during treatment and for at least 1 month after the last Eylea injection

☐ Women of childbearing potential must use effective contraception during treatment and for at least 3 months after the last Eylea injection

☐ Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus

☐ Eylea should never be used in pregnancy

☐ I don't know

The following questions ask about the Eylea injection procedure.

Q13. Should topical anaesthesia be used prior to the Eylea injection?

☐ Yes

☐ No

☐ I don't know

Q14. A disinfectant (e.g., povidone iodine solution) should be applied to the periocular skin, eyelid, and ocular surface.

☐ True

☐ False

☐ I don't know

Q15. After the disinfectant is applied, which of the following steps should be taken prior to marking the scleral injection site?

Tick <u>all</u> that apply.

☐ Cover the eye with a sterile drape

☐ Insert a sterile lid speculum

☐ Dilate the eye

☐ I don't know

Q16. In preparation for the Eylea injection, the eye should be marked at which of the following positions:

☐ At a distance 3.0 to 3.5 mm posterior to the limbus

☐ At a distance 3.5 to 4.0 mm posterior to the limbus

☐ At a distance 4.0 to 4.5 mm posterior to the limbus

☐ I don't know

Q17. How should the injection needle be inserted into the eye?

- ☐ Into the vitreous cavity, aiming to the anterior part of the globe to avoid injuring the retina
- ☐ Into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe
- ☐ Into the vitreous cavity, aiming towards the posterior surface of the lens
- ☐ Under the conjunctiva
- ☐ I don't know

The following questions ask about procedures following the Eylea injection.

Q18. How should physicians evaluate a patient's vision immediately after an Eylea injection?

- ☐ Using a standard eye chart (e.g., Snellen, Notation Monoyer, Letter Score, ETDRS, Decimal)
- ☐ By hand movements or counting fingers
- ☐ It is not necessary to evaluate a patient's vision immediately after an Eylea injection
- ☐ None of the above
- ☐ I don't know

Q19. An increase in intraocular pressure has been seen within 60 minutes after an injection with Eylea.

- ☐ True
- ☐ False
- ☐ I don't know

Q20. What should physicians do in relation to the potential of increased intraocular pressure immediately following an Eylea injection?

Tick <u>all</u> that apply.

- ☐ Ensure that sterile equipment is available to perform paracentesis if necessary
- ☐ Undertake appropriate monitoring if increased intraocular pressure is suspected (e.g., check for perfusion of the optic nerve head or tonometry)

☐ Nothing needs to be done because increased ocular pressure is normal and never harmful

☐ None of the above

☐ I don't know

Q21. After the Eylea injection, patients should be instructed to report any symptoms suggestive of which of the following conditions?

Tick <u>all</u> that apply.

☐ Intraocular inflammation

☐ Drooping eyelid

☐ Endophthalmitis

☐ None of the above

☐ I don't know

Q22. Which of the following signs or symptoms are known undesirable side effects of using Eylea?

Tick Yes, No, or I don't know for each description of signs or symptoms.

Description of Signs or Symptoms	**Yes, this is an undesirable effect**	**No, this not an undesirable effect**	**I don't Know**
a. Endophthalmitis			
b. Transient increased intraocular pressure			
c. Fever			
d. Cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities			
e. Tear or detachment of the retinal pigment epithelium			
f. Headache			

The following questions ask about information you have received about Eylea.

Q23. Please indicate whether you have received and/or reviewed the following Eylea informational material.

Materials	Have you received the material?	Have you reviewed the material?
Summary of Product Characteristics		
Eylea Prescriber Guide		
Intravitreal injection procedure video		
Patient Booklet including a Patient Information Audio CD and the Patient Information Leaflet		

[ONLY DISPLAY RESPONSES THAT WERE TICKED IN Q23; If the response option "Patient Booklet including a Patient Information Audio CD and Patient Information Leaflet" is ticked, then please display Patient Information Audio CD and Patient Information Leaflet as separate response options in the table below]

Q24. How helpful were these materials to you in treating and educating your patients?

Materials	Not at all helpful 1	2	3	Extremely helpful 4
Summary of Product Characteristics				
Eylea Prescriber Guide				
Intravitreal injection procedure video				
Patient Booklet				
Patient Information Audio CD				
Patient Information Leaflet				

Q25. In the past 3 months, to how many patients have you prescribed and/or <u>administered</u> Eylea for the following indications?

Indications	None	1 to 5 patients	6 to 10 patients	11 to 20 patients	More than 20 patients	I'm not sure
wAMD						
CRVO						
BRVO						
DME						
Other indications						

Q26. Considering the patients under your care who are receiving Eylea injections, to how many did you provide a Patient Booklet?

- ☐ All of my patients
- ☐ Most of my patients
- ☐ A few of my patients
- ☐ None of my patients [**IF Q26 = "None of my patients" SKIP TO Q28**]

Q27. When would you provide the Patient Booklet and discuss it with your patient?

Tick <u>all</u> that apply.

- ☐ Before the start of treatment with Eylea
- ☐ When a patient has an Eylea-related adverse event
- ☐ I do not reference the Patient Information Booklet
- ☐ Other

In this next section, please tell us a little about yourself and your clinical practice

Q28. What is your focus within ophthalmology?

Tick <u>all</u> that apply.

- ☐ Retina
- ☐ General ophthalmology
- ☐ Glaucoma
- ☐ Cataract
- ☐ Other

Q29. How many <u>anti-VEGF</u> intravitreal injections do you <u>administer</u> on average each month?

- ☐ Less than 5 per month
- ☐ 5 to 20 per month
- ☐ 21 to 40 per month
- ☐ More than 40 per month
- ☐ I don't know

Q30. When did you last <u>administer</u> an <u>Eylea</u> injection?

- ☐ Less than 1 month ago
- ☐ 1 to 3 months ago
- ☐ 4 to 6 months ago
- ☐ I don't know

Q31. How many years have you been treating patients?

- ☐ 5 years or fewer
- ☐ 6 to 10 years
- ☐ 11 to 15 years
- ☐ 16 to 20 years
- ☐ 21 to 25 years
- ☐ More than 25 years

Q32. Are you…?

☐ Male

☐ Female

Thank you for completing the questionnaire.

Reporting adverse events: Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax: 01635 563703, Email: phdsguk@bayer.co.uk

If you would like additional information or have any questions about the prescribing guidelines or safety information related to Eylea, please click on the link below to access the Eylea Prescriber Guide.

[INSERT LINK]

Annex 4. Patient Questionnaire

EYLEA® (Aflibercept Solution for Ocular Injection) Risk Minimisation Program Evaluation

Patient Questionnaire

Thank you for agreeing to take part in this study.

The purpose of this study is to learn more about what patients know about their eye injections. The results from the study will help us to improve the information that patients are given about an eye injection called Eylea.

The questionnaire should take about 10-15 minutes to complete. I will read the questions out to you one at a time, and then record your answers on this form.

Please remember that we are interested in learning what information you know about Eylea, rather than what has actually happened to you.

Inform the patient that the questions reference information that they might communicate with their ophthalmologist or anyone in the ophthalmologist's eye clinic, such as a nurse.

If needed, repeat the question.

Provide hard copy of table to patient as reference.

Q1. Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection?

Please answer:

☐ "Yes" if you think you need to tell your ophthalmologist, *OR*

☐ "No" if you think you do not need to tell your ophthalmologist, *OR*

☐ "I don't know" if you do not know or you are not sure.

What information should you tell your ophthalmologist about?		Yes	No	I don't know
a.	Any current eye problems (for example, infection, pain or redness in the eye)	☐	☐	☐
b.	Any allergies to medications (for example, iodine or painkillers)	☐	☐	☐
c.	Any problems with eye injections in the past	☐	☐	☐
d.	If you have glaucoma or have had issues with feeling of high pressure in the eye in the past	☐	☐	☐
e.	If you see flashes of light	☐	☐	☐
f.	If you see moving spots (known as floaters) in your eye	☐	☐	☐
g.	Any medications that you have used	☐	☐	☐
h.	If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection	☐	☐	☐
i.	If you are pregnant, are planning to become pregnant, or are breast feeding	☐	☐	☐

Q2. Just like any medicine, Eylea has the potential to cause side effects. Not everyone who receives an Eylea injection will experience a side effect.

I am going to read a list of side effects to you. For each side effect I want you to tell me:

☐ "Yes" if you think it is a possible side effect of Eylea, *OR*

☐ "No" if you think it is NOT a possible side effect of Eylea, *OR*

☐ "I don't know".

We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences.

If needed, repeat the question.

Provide hard copy of table to patient as reference.

Is […side-effect] a possible side effect of Eylea?		Yes	No	I don't know
a.	…a red or bloodshot eye	☐	☐	☐
b.	…nausea and vomiting (feeling or being sick)	☐	☐	☐
c.	…eye pain	☐	☐	☐
d.	…detachment of the gel-like substance inside the eye from the retina	☐	☐	☐
e.	…seeing halos around lights	☐	☐	☐
f.	…sudden flashes of light	☐	☐	☐
g.	…sudden appearance or increase in moving spots (known as floaters)	☐	☐	☐
h.	…cloudy or blurred vision	☐	☐	☐
i.	…sensitivity to light	☐	☐	☐
j.	…an eye infection	☐	☐	☐

Q3. What should you do if you think you might be having a side effect from your Eylea injection?

- ☐ Speak to your ophthalmologist (or someone in his or her office) immediately
- ☐ Wait 48 hours to see if the symptoms improve
- ☐ None of the above
- ☐ I don't know

The next few questions ask about any information that you may have had from your ophthalmologist about Eylea.

Q4. Before your first injection of Eylea, did your ophthalmologist (or someone in his or her office) tell you what to expect during and after the injection?

- ☐ Yes
- ☐ No
- ☐ I don't know or I don't remember

Q5. For the next question, I am going to show you some information materials. For each item, please tell me if you have been given it or not.

Show the patient each piece of material.

Eylea Materials	Have you been given this material?		
	Yes	No	I don't know or I don't remember
Patient Booklet, "Your Guide to EYLEA"	☐	☐	☐
Audio CD	☐	☐	☐
Patient Information Leaflet	☐	☐	☐

Q6a. Did your ophthalmologist (or someone in his or her office) give you any other information materials about Eylea that are not included here?

☐ Yes → **if yes, ask Q6b**

☐ No → **if no, go to Q7**

☐ I don't know or I don't remember

[Skip instruction: if Q6a is "Yes", ask Q6b; if Q6a is "No", go to Q7.]

Q6b. What else did they give you?

_____

_____

_____

[Skip instruction: if the patient reported that they were not given any materials, then go to Q10; otherwise ask Q7.]

Show the patient each piece of material that they have received based on response to Q5 and Q6b.

Q7. Did you read or listen to any of the Eylea materials?

Eylea Materials	Did you read or listen to the Eylea material?		
	Yes	No	I don't know or I don't remember
Patient Booklet, "Your Guide to EYLEA"	☐	☐	☐
Audio CD	☐	☐	☐
Patient Information Leaflet	☐	☐	☐

Fill in and ask about item(s) from Q6b, if applicable.

[Skip instruction: if the patient responded "I don't know or I don't remember" to all materials, go to Q9.]

Show the patient only the materials they have read from Q7.

Q8. Which of these Eylea information materials did you find the most useful?

(Please choose one answer only.)

- ☐ Patient Booklet, "Your Guide to EYLEA"
- ☐ Audio CD
- ☐ Patient Information Leaflet

Fill in and ask about item(s) from Q6b, if applicable.

- ☐ _____

_____

- ☐ None
- ☐ I don't know or I don't remember

[Skip instruction: go to Q10.]

Q9. We would be interested in understanding any reasons that you did not read or listen to any of the Eylea information materials.

Let the patient respond and then select the response choices that fit. If needed, read response choices to the patient.

(Please choose all that apply.)

- ☐ You lost the materials
- ☐ Someone else explained the information to you
- ☐ You already knew the information
- ☐ You don't typically read or listen to materials given to you by your doctor
- ☐ You couldn't read them due to problems with your vision
- ☐ The materials were too difficult to understand
- ☐ The materials were too long
- ☐ Other [specify] _____

_____

- ☐ I don't know or I don't remember

The last questions ask for information that will help us to describe the participants completing this questionnaire.

Q10. How old are you?

- ☐ 18 – 25 years
- ☐ 26 – 35 years
- ☐ 36 – 45 years
- ☐ 46 – 55 years
- ☐ 56 – 65 years
- ☐ 66 – 75 years
- ☐ 76 – 85 years
- ☐ 86 years or older

Allow the patient to answer Q11 without reading the response options. If they are unable to answer the question, then read each of the response options.

Q11. What is the highest level of education you have completed?

(Please choose one answer only.)

- ☐ Primary school education or less
- ☐ Secondary school education (e.g., CSE, O level, A level)
- ☐ Professional or work-related college qualifications (e.g. City and Guilds, Certificate of Higher Education)
- ☐ Undergraduate university degree (e.g., BSc/BA)
- ☐ Postgraduate university degree (e.g., MSc/MA, PhD)

Additional Scottish examples to use if appropriate: Scottish Standard Grades or Higher.

Additional examples to use if appropriate: Diploma of Higher Education, foundation degree.

If needed, repeat the question. Don't read the option "I don't know" to the patient. If the patient does not know the answer, then select "I don't know"

Q12. We are interested in knowing if you receive any help from anyone other than your doctor or nurse (e.g., a family member, friend, or caregiver) in relation to your eye treatment.

	None of the time	Some of the time	Most of the time	All of the time	I don't know
How often do you need to have someone other than your doctor or nurse READ information materials to you?	☐	☐	☐	☐	☐
How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you?	☐	☐	☐	☐	☐
How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you?	☐	☐	☐	☐	☐

Thank you for taking time to take part in this study. If you have any questions about the safety of treatment with eye injections, you should talk with your ophthalmologist.

Annex 5. Analysis Tables for Non-recruiting Physicians (Overall and by Country)

Tables

Table 1. Physician Experience With Aflibercept, Overall and by Country

Question	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Have you prescribed Eylea and/or administered an Eylea injection any patient in the past 6 months? (S1) Tick all that apply.						
Prescribed Eylea	66 (96)	54 (92)	84 (85)	93 (91)	93 (94)	390 (91)
Administered an Eylea injection	62 (90)	48 (81)	67 (68)	93 (91)	85 (86)	355 (83)
For which of the following indications have you prescribed and/or administered Eylea in the past 6 months? (S2) Tick all that apply.						
Neovascular (wet) age-related macular degeneration (wAMD)	67 (97)	58 (98)	94 (95)	100 (98)	97 (98)	416 (97)
Visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO)	61 (88)	49 (83)	41 (41)	62 (61)	73 (74)	286 (67)
Visual impairment due to diabetic macular oedema (DME)	64 (93)	51 (86)	63 (64)	90 (88)	72 (73)	340 (79)
Visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)	54 (78)	45 (76)	37 (37)	58 (57)	53 (54)	247 (58)
Other indication	4 (6)	6 (10)	2 (2)	16 (16)	3 (3)	31 (7)
At your site, who has the primary responsibility for the preparation of an Eylea injection (i.e., opens the vial or pre-filled syringe[a] and prepares the syringe for injection)? (S4) Tick one answer.						
I am responsible	55 (80)	33 (56)	45 (45)	36 (35)	64 (65)	233 (54)
A specialized nurse	9 (13)	19 (32)	48 (48)	16 (16)	32 (32)	124 (29)
Pharmacy	1 (1)	5 (8)	3 (3)	50 (49)	3 (3)	62 (14)
Laboratory	2 (3)	0 (0)	1 (1)	0 (0)	0 (0)	3 (1)
Other	2 (3)	2 (3)	2 (2)	0 (0)	0 (0)	6 (1)
In the past 3 months, to how many patients have you prescribed and/or administered Eylea for the following indications? (Q25)						
wAMD						
None	0 (0)	0 (0)	4 (4)	1 (1)	1 (1)	6 (1)

Table 1. Physician Experience With Aflibercept, Overall and by Country

Question	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
1 to 5 patients	6 (9)	4 (7)	26 (26)	23 (23)	15 (15)	74 (17)
6 to 10 patients	6 (9)	6 (10)	14 (14)	16 (16)	12 (12)	54 (13)
11 to 20 patients	16 (23)	10 (17)	18 (18)	18 (18)	15 (15)	77 (18)
More than 20 patients	40 (58)	37 (63)	31 (31)	41 (40)	53 (54)	202 (47)
I'm not sure	0 (0)	1 (2)	3 (3)	0 (0)	1 (1)	5 (1)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
CRVO						
None	4 (6)	2 (3)	30 (30)	24 (24)	17 (17)	77 (18)
1 to 5 patients	29 (42)	26 (44)	37 (37)	41 (40)	30 (30)	163 (38)
6 to 10 patients	15 (22)	12 (20)	9 (9)	13 (13)	17 (17)	66 (15)
11 to 20 patients	9 (13)	8 (14)	9 (9)	8 (8)	15 (15)	49 (11)
More than 20 patients	10 (14)	8 (14)	6 (6)	9 (9)	16 (16)	49 (11)
I'm not sure	1 (1)	2 (3)	5 (5)	1 (1)	2 (2)	11 (3)
No answer	1 (1)	1 (2)	3 (3)	6 (6)	2 (2)	13 (3)
BRVO						
None	4 (6)	4 (7)	31 (31)	23 (23)	31 (31)	93 (22)
1 to 5 patients	27 (39)	23 (39)	36 (36)	37 (36)	26 (26)	149 (35)
6 to 10 patients	16 (23)	12 (20)	12 (12)	18 (18)	15 (15)	73 (17)
11 to 20 patients	10 (14)	8 (14)	4 (4)	5 (5)	9 (9)	36 (8)
More than 20 patients	9 (13)	9 (15)	8 (8)	11 (11)	11 (11)	48 (11)
I'm not sure	0 (0)	2 (3)	5 (5)	2 (2)	4 (4)	13 (3)
No answer	3 (4)	1 (2)	3 (3)	6 (6)	3 (3)	16 (4)
DME						
None	3 (4)	4 (7)	20 (20)	10 (10)	14 (14)	51 (12)
1 to 5 patients	16 (23)	10 (17)	25 (25)	20 (20)	23 (23)	94 (22)
6 to 10 patients	16 (23)	10 (17)	13 (13)	21 (21)	18 (18)	78 (18)
11 to 20 patients	13 (19)	12 (20)	12 (12)	24 (24)	13 (13)	74 (17)
More than 20 patients	20 (29)	21 (36)	23 (23)	24 (24)	26 (26)	114 (27)
I'm not sure	0 (0)	1 (2)	2 (2)	0 (0)	3 (3)	6 (1)
No answer	1 (1)	1 (2)	4 (4)	3 (3)	2 (2)	11 (3)
Other indications						

Table 1. Physician Experience With Aflibercept, Overall and by Country

Question	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
None	49 (71)	33 (56)	60 (61)	50 (49)	71 (72)	263 (61)
1 to 5 patients	11 (16)	5 (8)	6 (6)	17 (17)	10 (10)	49 (11)
6 to 10 patients	1 (1)	2 (3)	1 (1)	4 (4)	1 (1)	9 (2)
11 to 20 patients	0 (0)	4 (7)	3 (3)	3 (3)	2 (2)	12 (3)
More than 20 patients	1 (1)	1 (2)	2 (2)	4 (4)	1 (1)	9 (2)
I'm not sure	1 (1)	9 (15)	18 (18)	17 (17)	11 (11)	56 (13)
No answer	6 (9)	5 (8)	9 (9)	7 (7)	3 (3)	30 (7)
How many anti-VEGF intravitreal injections do you administer on average each month? (Q29)						
Less than 5 per month	5 (7)	2 (3)	15 (15)	6 (6)	15 (15)	43 (10)
5 to 20 per month	14 (20)	13 (22)	38 (38)	34 (33)	24 (24)	123 (29)
21 to 40 per month	24 (35)	11 (19)	18 (18)	29 (28)	17 (17)	99 (23)
More than 40 per month	23 (33)	31 (53)	20 (20)	29 (28)	40 (40)	143 (33)
I don’t know	2 (3)	1 (2)	5 (5)	1 (1)	1 (1)	10 (2)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
When did you last administer an Eylea injection? (Q30)						
Less than 1 month ago	61 (88)	53 (90)	71 (72)	83 (81)	69 (70)	337 (79)
1 to 3 months ago	1 (1)	2 (3)	11 (11)	12 (12)	19 (19)	45 (11)
4 to 6 months ago	3 (4)	1 (2)	7 (7)	4 (4)	4 (4)	19 (4)
I don’t know	3 (4)	2 (3)	7 (7)	0 (0)	5 (5)	17 (4)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)

[a]The pre-filled syringe option was not on the market at the time the survey was conducted

Table 2. Physician Characteristics, Overall and by Country

Question	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
What is your focus within ophthalmology? (Q28) Tick all that apply.						
Retina	50 (72)	45 (76)	67 (68)	79 (77)	77 (78)	318 (74)
General ophthalmology	36 (52)	43 (73)	50 (51)	48 (47)	52 (53)	229 (54)
Glaucoma	24 (35)	26 (44)	31 (31)	43 (42)	26 (26)	150 (35)
Cataract	30 (43)	32 (54)	36 (36)	50 (49)	46 (46)	194 (45)
Other	2 (3)	3 (5)	9 (9)	13 (13)	9 (9)	36 (8)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
How many years have you been treating patients? (Q31)						
5 years or fewer	8 (12)	0 (0)	19 (19)	9 (9)	9 (9)	45 (11)
6 to 10 years	19 (28)	12 (20)	32 (32)	29 (28)	31 (31)	123 (29)
11 to 15 years	14 (20)	15 (25)	11 (11)	21 (21)	21 (21)	82 (19)
16 to 20 years	17 (25)	12 (20)	15 (15)	27 (26)	15 (15)	86 (20)
21 to 25 years	5 (7)	10 (17)	6 (6)	7 (7)	12 (12)	40 (9)
More than 25 years	5 (7)	9 (15)	13 (13)	6 (6)	9 (9)	42 (10)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
Are you…? (Q32)						
Male	53 (77)	45 (76)	78 (79)	54 (53)	81 (82)	311 (73)
Female	15 (22)	13 (22)	18 (18)	45 (44)	16 (16)	107 (25)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)

Table 3-1. Physician Knowledge: Storage and Preparation, Overall and by Country

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
Eylea is a suspension, which contains particulates and is cloudy						
Yes, this is true	16 (23)	8 (14)	13 (13)	10 (10)	15 (15)	62 (14)
No, this is not true*	45 (65) [53 - 76]	46 (78) [65 - 88]	71 (72) [62 - 80]	84 (82) [74 - 89]	71 (72) [62 - 80]	317 (74) [70 - 78]
I don't know	8 (12)	5 (8)	15 (15)	8 (8)	13 (13)	49 (11)
For the intravitreal injection, a 30-gauge x ½ inch injection needle should be used						
Yes, this is true*	60 (87) [77 - 94]	51 (86) [75 - 94]	83 (84) [75 - 90]	101 (99) [95 - 100]	87 (88) [80 - 94]	382 (89) [86 - 92]
No, this is not true	5 (7)	4 (7)	7 (7)	1 (1)	4 (4)	21 (5)
I don't know	4 (6)	4 (7)	9 (9)	0 (0)	8 (8)	25 (6)
Adequate anaesthesia and asepsis (e.g., use of povidone iodine) must be provided for the patient						
Yes, this is true*	67 (97) [90 - 100]	58 (98) [91 - 100]	92 (93) [86 - 97]	102 (100) [96 - 100]	98 (99) [95 - 100]	417 (97) [95 - 99]
No, this is not true	0 (0)	1 (2)	6 (6)	0 (0)	0 (0)	7 (2)
I don't know	2 (3)	0 (0)	1 (1)	0 (0)	1 (1)	4 (1)
Number of correct responses selected among the three Yes/No questions listed above						
0	0 (0)	0 (0)	2 (2)	0 (0)	1 (1)	3 (1)
1	7 (10)	3 (5)	6 (6)	1 (1)	5 (5)	22 (5)
2	21 (30)	16 (27)	33 (33)	17 (17)	28 (28)	115 (27)
3	41 (59)	40 (68)	58 (59)	84 (82)	65 (66)	288 (67)
The next three questions were only asked of those physicians who indicated they use the vial						
Not applicable skip pattern	19	25	57	38	36	175
The vial of Eylea is reusable between patients and can be used for multiple injections						
Yes, this is true	2 (4)	1 (3)	3 (7)	24 (38)	2 (3)	32 (13)
No, this is not true*	44 (88) [76 - 95]	32 (94) [80 - 99]	38 (90) [77 - 97]	34 (53) [40 - 66]	60 (95) [87 - 99]	208 (82) [77 - 87]
I don't know	3 (6)	0 (0)	1 (2)	5 (8)	1 (2)	10 (4)
No answer	1 (2)	1 (3)	0 (0)	1 (2)	0 (0)	3 (1)
The vial of Eylea must be stored in the refrigerator (2°C to 8°C)						
Yes, this is true*	45 (90) [78 - 97]	30 (88) [73 - 97]	35 (83) [69 - 93]	56 (88) [77 - 94]	46 (73) [60 - 83]	212 (84) [79 - 88]
No, this is not true	3 (6)	3 (9)	2 (5)	2 (3)	7 (11)	17 (7)
I don't know	1 (2)	1 (3)	5 (12)	6 (9)	10 (16)	23 (9)
No answer	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours						
Yes, this is true	19 (38)	9 (26)	12 (29)	20 (31)	13 (21)	73 (29)
No, this is not true*	18 (36) [23 - 51]	17 (50) [32 - 68]	16 (38) [24 - 54]	21 (33) [22 - 46]	33 (52) [39 - 65]	105 (42) [35 - 48]
I don't know	12 (24)	8 (24)	14 (33)	23 (36)	17 (27)	74 (29)
No answer	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)

Table 3-1. Physician Knowledge: Storage and Preparation, Overall and by Country

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
Number of correct responses selected among the three Yes/No questions listed above						
0	1 (2)	0 (0)	1 (2)	5 (8)	0 (0)	7 (3)
1	6 (12)	5 (15)	8 (19)	16 (25)	15 (24)	50 (20)
2	28 (56)	13 (38)	18 (43)	34 (53)	20 (32)	113 (45)
3	15 (30)	16 (47)	15 (36)	9 (14)	28 (44)	83 (33)

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
What is the recommended dose for Eylea? (Q2)						
12.5 microlitres (0.5 mg)	9 (13)	3 (5)	18 (18)	24 (24)	13 (13)	67 (16)
50 microlitres (2 mg)*	47 (68) [56 - 79]	49 (83) [71 - 92]	68 (69) [59 - 78]	67 (66) [56 - 75]	82 (83) [74 - 90]	313 (73) [69 - 77]
90 microlitres (3.6 mg)	0 (0)	2 (3)	1 (1)	1 (1)	1 (1)	5 (1)
100 microlitres (4 mg)	6 (9)	3 (5)	3 (3)	3 (3)	1 (1)	16 (4)
I don't know	7 (10)	2 (3)	7 (7)	7 (7)	1 (1)	24 (6)
No answer	0 (0)	0 (0)	2 (2)	0 (0)	1 (1)	3 (1)
For each of the following statements related to the Eylea dosing and monitoring recommendations for the treatment of wAMD, please indicate if the statement is true, not true, or if you do not know. (Q3)						
Not applicable skip pattern (did not tick wAMD in screener question 2)	2	1	5	2	2	12
During the first 12 months, treatment is initiated with one injection per month for three consecutive doses, followed by one injection every 2 months.						
Yes, this is true*	58 (87) [76 - 94]	54 (93) [83 - 98]	83 (88) [80 - 94]	95 (95) [89 - 98]	88 (91) [83 - 96]	378 (91) [88 - 93]
No, this is not true	7 (10)	4 (7)	5 (5)	3 (3)	7 (7)	26 (6)
I don't know	1 (1)	0 (0)	2 (2)	1 (1)	1 (1)	5 (1)
No answer	1 (1)	0 (0)	4 (4)	1 (1)	1 (1)	7 (2)
During the first 12 months, there is no requirement for monitoring between injections.						
Yes, this is true*	27 (40) [28 - 53]	14 (24) [14 - 37]	24 (26) [17 - 36]	24 (24) [16 - 34]	28 (29) [20 - 39]	117 (28) [24 - 33]
No, this is not true	38 (57)	44 (76)	65 (69)	70 (70)	66 (68)	283 (68)
I don't know	1 (1)	0 (0)	2 (2)	3 (3)	2 (2)	8 (2)
No answer	1 (1)	0 (0)	3 (3)	3 (3)	1 (1)	8 (2)
After the first 12 months, the treatment interval may be extended based on visual and anatomical outcomes.						
Yes, this is true*	62 (93) [83 - 98]	56 (97) [88 - 100]	85 (90) [83 - 96]	96 (96) [90 - 99]	91 (94) [87 - 98]	390 (94) [91 - 96]
No, this is not true	4 (6)	1 (2)	3 (3)	2 (2)	3 (3)	13 (3)
I don't know	0 (0)	1 (2)	2 (2)	1 (1)	2 (2)	6 (1)
No answer	1 (1)	0 (0)	4 (4)	1 (1)	1 (1)	7 (2)
After the first 12 months, the schedule for monitoring should be determined by the treating physician and may be more frequent than the schedule of injections.						
Yes, this is true*	59 (88) [78 - 95]	51 (88) [77 - 95]	70 (74) [64 - 83]	80 (80) [71 - 87]	81 (84) [75 - 90]	341 (82) [78 - 86]
No, this is not true	5 (7)	3 (5)	11 (12)	11 (11)	14 (14)	44 (11)
I don't know	2 (3)	4 (7)	9 (10)	8 (8)	1 (1)	24 (6)
No answer	1 (1)	0 (0)	4 (4)	1 (1)	1 (1)	7 (2)
Number of correct responses selected among the four Yes/No questions listed above						

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
0	1 (1)	1 (2)	4 (4)	2 (2)	1 (1)	9 (2)
1	3 (4)	1 (2)	5 (5)	2 (2)	4 (4)	15 (4)
2	7 (10)	6 (10)	14 (15)	17 (17)	16 (16)	60 (14)
3	35 (52)	38 (66)	55 (59)	57 (57)	52 (54)	237 (57)
4	21 (31)	12 (21)	16 (17)	22 (22)	24 (25)	95 (23)
For each of the following statements related to the Eylea dosing recommendations for the treatment of macular oedema secondary to CRVO or BRVO, please indicate if the statement is true, not true, or if you do not know. (Q4)						
Not applicable skip pattern (did not tick CRVO or BRVO in screener question 2)	6	8	52	32	23	121
After the initial injection, treatment is given monthly.						
Yes, this is true*	41 (65) [52 - 77]	27 (53) [38 - 67]	32 (68) [53 - 81]	45 (64) [52 - 75]	43 (57) [45 - 68]	188 (61) [56 - 67]
No, this is not true	21 (33)	22 (43)	12 (26)	22 (31)	30 (39)	107 (35)
I don't know	1 (2)	2 (4)	3 (6)	1 (1)	2 (3)	9 (3)
No answer	0 (0)	0 (0)	0 (0)	2 (3)	1 (1)	3 (1)
The interval between two doses should not be shorter than 2 months.						
Yes, this is true	17 (27)	8 (16)	20 (43)	15 (21)	18 (24)	78 (25)
No, this is not true*	44 (70) [57 - 81]	42 (82) [69 - 92]	22 (47) [32 - 62]	50 (71) [59 - 82]	54 (71) [60 - 81]	212 (69) [64 - 74]
I don't know	2 (3)	1 (2)	5 (11)	3 (4)	3 (4)	14 (5)
No answer	0 (0)	0 (0)	0 (0)	2 (3)	1 (1)	3 (1)
If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued.						
Yes, this is true*	50 (79) [67 - 89]	47 (92) [81 - 98]	33 (70) [55 - 83]	57 (81) [70 - 90]	63 (83) [73 - 91]	250 (81) [77 - 86]
No, this is not true	8 (13)	2 (4)	11 (23)	10 (14)	11 (14)	42 (14)
I don't know	5 (8)	2 (4)	3 (6)	1 (1)	1 (1)	12 (4)
No answer	0 (0)	0 (0)	0 (0)	2 (3)	1 (1)	3 (1)
Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity.						
Yes, this is true*	50 (79) [67 - 89]	43 (84) [71 - 93]	32 (68) [53 - 81]	56 (80) [69 - 89]	62 (82) [71 - 90]	243 (79) [74 - 84]
No, this is not true	11 (17)	8 (16)	14 (30)	10 (14)	11 (14)	54 (18)
I don't know	2 (3)	0 (0)	1 (2)	2 (3)	2 (3)	7 (2)
No answer	0 (0)	0 (0)	0 (0)	2 (3)	1 (1)	3 (1)
Number of correct responses selected among the four Yes/No questions listed above						
0	1 (2)	1 (2)	1 (2)	2 (3)	2 (3)	7 (2)
1	5 (8)	2 (4)	6 (13)	6 (9)	2 (3)	21 (7)

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
2	12 (19)	7 (14)	15 (32)	10 (14)	16 (21)	60 (20)
3	24 (38)	21 (41)	17 (36)	26 (37)	36 (47)	124 (40)
4	21 (33)	20 (39)	8 (17)	26 (37)	20 (26)	95 (31)
For each of the following statements related to the Eylea dosing recommendations for the treatment of DME, please indicate if the statement is true, not true, or if you do not know. (Q5)						
Not applicable skip pattern (did not tick DME in screener question 2)	5	8	36	12	27	88
Eylea treatment is initiated with one injection per month for five consecutive doses.						
Yes, this is true*	48 (75) [63 - 85]	39 (76) [63 - 87]	36 (57) [44 - 70]	58 (64) [54 - 74]	59 (82) [71 - 90]	240 (71) [65 - 75]
No, this is not true	14 (22)	8 (16)	25 (40)	27 (30)	12 (17)	86 (25)
I don't know	1 (2)	4 (8)	1 (2)	3 (3)	0 (0)	9 (3)
No answer	1 (2)	0 (0)	1 (2)	2 (2)	1 (1)	5 (1)
After the first 5 months, Eylea treatment is followed by one injection every 2 months.						
Yes, this is true*	45 (70) [58 - 81]	39 (76) [63 - 87]	39 (62) [49 - 74]	67 (74) [64 - 83]	57 (79) [68 - 88]	247 (73) [68 - 77]
No, this is not true	15 (23)	8 (16)	21 (33)	17 (19)	11 (15)	72 (21)
I don't know	2 (3)	4 (8)	2 (3)	4 (4)	3 (4)	15 (4)
No answer	2 (3)	0 (0)	1 (2)	2 (2)	1 (1)	6 (2)
During the first 12 months, there is no requirement for monitoring between injections.						
Yes, this is true*	23 (36) [24 - 49]	15 (29) [17 - 44]	11 (17) [9 - 29]	22 (24) [16 - 35]	16 (22) [13 - 34]	87 (26) [21 - 31]
No, this is not true	38 (59)	36 (71)	50 (79)	63 (70)	53 (74)	240 (71)
I don't know	2 (3)	0 (0)	1 (2)	3 (3)	2 (3)	8 (2)
No answer	1 (2)	0 (0)	1 (2)	2 (2)	1 (1)	5 (1)
Number of correct responses selected among the three Yes/No questions listed above						
0	11 (17)	8 (16)	14 (22)	17 (19)	9 (13)	59 (17)
1	9 (14)	6 (12)	17 (27)	17 (19)	10 (14)	59 (17)
2	25 (39)	24 (47)	27 (43)	38 (42)	37 (51)	151 (44)
3	19 (30)	13 (25)	5 (8)	18 (20)	16 (22)	71 (21)
The Eylea vial contains more than the recommended dose of Eylea and excess volume should be expelled before injecting. (Q8)						
True*	47 (94) [83 - 99]	31 (91) [76 - 98]	35 (83) [69 - 93]	48 (75) [63 - 85]	60 (95) [87 - 99]	221 (87) [83 - 91]
False	2 (4)	2 (6)	4 (10)	11 (17)	3 (5)	22 (9)
I don't know	1 (2)	1 (3)	2 (5)	4 (6)	0 (0)	8 (3)
No answer	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	2 (1)
Not applicable skip pattern	19	25	57	38	36	175

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
After removing all of the drug from the Eylea vial with a syringe, the plunger of the syringe should be depressed until the tip aligns with the line that marks which number of millilitres (ml) on the syringe? (Q9)						
0.05 ml*	33 (66) [51 - 79]	26 (76) [59 - 89]	22 (52) [36 - 68]	41 (64) [51 - 76]	48 (76) [64 - 86]	170 (67) [61 - 73]
0.1 ml	4 (8)	1 (3)	4 (10)	5 (8)	4 (6)	18 (7)
0.15 ml	0 (0)	1 (3)	0 (0)	0 (0)	1 (2)	2 (1)
0.2 ml	4 (8)	3 (9)	4 (10)	2 (3)	1 (2)	14 (6)
0.5 ml	8 (16)	2 (6)	7 (17)	9 (14)	7 (11)	33 (13)
I don't know	1 (2)	1 (3)	4 (10)	6 (9)	2 (3)	14 (6)
No answer	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	2 (1)
Not applicable skip pattern	19	25	57	38	36	175

Table 3-3. Physician Knowledge: Safe Use, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
What should you do to prepare the patient before the start of treatment with Eylea? (Q10) Tick all that apply.						
Provide the Patient Booklet which includes a Patient Information Audio CD and Patient Information Leaflet*	41 (59) [47 - 71]	27 (46) [33 - 59]	63 (64) [53 - 73]	44 (43) [33 - 53]	95 (96) [90 - 99]	270 (63) [58 - 68]
Explain the implications of anti-VEGF treatment*	64 (93) [84 - 98]	56 (95) [86 - 99]	86 (87) [79 - 93]	98 (96) [90 - 99]	98 (99) [95 - 100]	402 (94) [91 - 96]
Inform the patient to report any signs and symptoms potentially associated with serious adverse events and provide information on when to seek medical attention*	63 (91) [82 - 97]	56 (95) [86 - 99]	89 (90) [82 - 95]	94 (92) [85 - 97]	96 (97) [91 - 99]	398 (93) [90 - 95]
None of the above	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (0)
I don't know	0 (0)	1 (2)	1 (1)	0 (0)	0 (0)	2 (0)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
Selected all three of the correct responses	40 (58) [45 - 70]	27 (46) [33 - 59]	62 (63) [52 - 72]	42 (41) [32 - 51]	93 (94) [87 - 98]	264 (62) [57 - 66]
Selected at least two of the three correct responses	60 (87) [77 - 94]	55 (93) [84 - 98]	82 (83) [74 - 90]	94 (92) [85 - 97]	98 (99) [95 - 100]	389 (91) [88 - 93]
Selected at least one of the three correct responses	68 (99) [92 - 100]	57 (97) [88 - 100]	94 (95) [89 - 98]	100 (98) [93 - 100]	98 (99) [95 - 100]	417 (97) [95 - 99]
Eylea is contraindicated in which of the following patients? (Q11) Tick all that apply.						
Patients with a known hypersensitivity to Eylea or to any of the excipients (e.g., non-active ingredients)*	64 (93) [84 - 98]	56 (95) [86 - 99]	91 (92) [85 - 96]	98 (96) [90 - 99]	96 (97) [91 - 99]	405 (95) [92 - 97]
Patients with active or suspected ocular or periocular infection*	66 (96) [88 - 99]	52 (88) [77 - 95]	88 (89) [81 - 94]	97 (95) [89 - 98]	93 (94) [87 - 98]	396 (93) [90 - 95]
Patients with high blood pressure	9 (13)	3 (5)	11 (11)	8 (8)	14 (14)	45 (11)
Patients with active severe intraocular inflammation*	54 (78) [67 - 87]	51 (86) [75 - 94]	89 (90) [82 - 95]	87 (85) [77 - 92]	82 (83) [74 - 90]	363 (85) [81 - 88]
None of the above	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (0)
I don't know	0 (0)	2 (3)	1 (1)	0 (0)	0 (0)	3 (1)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
Selected all three of the correct responses	53 (77) [65 - 86]	48 (81) [69 - 90]	84 (85) [76 - 91]	86 (84) [76 - 91]	78 (79) [69 - 86]	349 (82) [78 - 85]
Selected at least two of the three correct responses	63 (91) [82 - 97]	55 (93) [84 - 98]	90 (91) [83 - 96]	96 (94) [88 - 98]	95 (96) [90 - 99]	399 (93) [90 - 95]
Selected at least one of the three correct responses	68 (99) [92 - 100]	56 (95) [86 - 99]	94 (95) [89 - 98]	100 (98) [93 - 100]	98 (99) [95 - 100]	416 (97) [95 - 99]
What is the recommended use of Eylea in women of childbearing potential? (Q12) Tick all that apply.						
Women of childbearing potential must use effective contraception during treatment and for at least 1 month after the last Eylea injection	12 (17)	7 (12)	8 (8)	7 (7)	4 (4)	38 (9)
Women of childbearing potential must use effective contraception during treatment and for at least 3 months after the last Eylea injection*	37 (54) [41 - 66]	27 (46) [33 - 59]	33 (33) [24 - 44]	54 (53) [43 - 63]	54 (55) [44 - 65]	205 (48) [43 - 53]
Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus*	36 (52) [40 - 64]	40 (68) [54 - 79]	50 (51) [40 - 61]	69 (68) [58 - 77]	59 (60) [49 - 69]	254 (59) [55 - 64]
Eylea should never be used in pregnancy	23 (33)	15 (25)	37 (37)	17 (17)	23 (23)	115 (27)
I don't know	9 (13)	6 (10)	8 (8)	12 (12)	12 (12)	47 (11)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)

Table 3-3. Physician Knowledge: Safe Use, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
Selected both of the correct responses	22 (32) [21 - 44]	23 (39) [27 - 53]	16 (16) [10 - 25]	40 (39) [30 - 49]	36 (36) [27 - 47]	137 (32) [28 - 37]
Selected at least one of the two correct responses	51 (74) [62 - 84]	44 (75) [62 - 85]	67 (68) [58 - 77]	83 (81) [72 - 88]	77 (78) [68 - 86]	322 (75) [71 - 79]

Table 3-4. Physician Knowledge: Injection Procedure, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
Should topical anaesthesia be used prior to the Eylea injection? (Q13)						
Yes*	62 (90) [80 - 96]	54 (92) [81 - 97]	90 (91) [83 - 96]	100 (98) [93 - 100]	96 (97) [91 - 99]	402 (94) [91 - 96]
No	6 (9)	2 (3)	5 (5)	0 (0)	1 (1)	14 (3)
I don't know	0 (0)	2 (3)	1 (1)	0 (0)	1 (1)	4 (1)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
A disinfectant (e.g., povidone iodine solution) should be applied to the periocular skin, eyelid, and ocular surface. (Q14)						
True*	67 (97) [90 - 100]	53 (90) [79 - 96]	91 (92) [85 - 96]	100 (98) [93 - 100]	98 (99) [95 - 100]	409 (96) [93 - 97]
False	1 (1)	4 (7)	2 (2)	0 (0)	0 (0)	7 (2)
I don't know	0 (0)	1 (2)	3 (3)	0 (0)	0 (0)	4 (1)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
After the disinfectant is applied, which of the following steps should be taken prior to marking the scleral injection site? (Q15) Tick all that apply.						
Cover the eye with a sterile drape*	61 (88) [78 - 95]	55 (93) [84 - 98]	79 (80) [71 - 87]	87 (85) [77 - 92]	84 (85) [76 - 91]	366 (86) [82 - 89]
Insert a sterile lid speculum*	63 (91) [82 - 97]	56 (95) [86 - 99]	79 (80) [71 - 87]	88 (86) [78 - 92]	92 (93) [86 - 97]	378 (88) [85 - 91]
Dilate the eye	6 (9)	26 (44)	41 (41)	17 (17)	28 (28)	118 (28)
I don't know	0 (0)	1 (2)	1 (1)	0 (0)	0 (0)	2 (0)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
Selected both of the correct responses	56 (81) [70 - 90]	54 (92) [81 - 97]	65 (66) [55 - 75]	76 (75) [65 - 83]	79 (80) [71 - 87]	330 (77) [73 - 81]
Selected at least one of the two correct responses	68 (99) [92 - 100]	57 (97) [88 - 100]	93 (94) [87 - 98]	99 (97) [92 - 99]	97 (98) [93 - 100]	414 (97) [95 - 98]
In preparation for the Eylea injection, the eye should be marked at which of the following positions: (Q16)						
At a distance 3.0 to 3.5 mm posterior to the limbus	6 (9)	12 (20)	9 (9)	11 (11)	4 (4)	42 (10)
At a distance 3.5 to 4.0 mm posterior to the limbus*	59 (86) [75 - 93]	44 (75) [62 - 85]	79 (80) [71 - 87]	87 (85) [77 - 92]	88 (89) [81 - 94]	357 (83) [80 - 87]
At a distance 4.0 to 4.5 mm posterior to the limbus	2 (3)	0 (0)	3 (3)	2 (2)	4 (4)	11 (3)
I don't know	1 (1)	2 (3)	5 (5)	0 (0)	2 (2)	10 (2)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
How should the injection needle be inserted into the eye? (Q17)						
Into the vitreous cavity, aiming to the anterior part of the globe to avoid injuring the retina	3 (4)	8 (14)	7 (7)	2 (2)	3 (3)	23 (5)
Into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe*	61 (88) [78 - 95]	46 (78) [65 - 88]	83 (84) [75 - 90]	96 (94) [88 - 98]	89 (90) [82 - 95]	375 (88) [84 - 91]
Into the vitreous cavity, aiming towards the posterior surface of the lens	3 (4)	1 (2)	2 (2)	2 (2)	4 (4)	12 (3)
Under the conjunctiva	0 (0)	0 (0)	2 (2)	0 (0)	0 (0)	2 (0)
I don't know	1 (1)	3 (5)	2 (2)	0 (0)	2 (2)	8 (2)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)

Table 3-5. Physician Knowledge: Side Effects, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
How should physicians evaluate a patient's vision immediately after an Eylea injection? (Q18)						
Using a standard eye chart (e.g., Snellen, Notation Monoyer, Letter Score, ETDRS, Decimal)	4 (6)	9 (15)	17 (17)	8 (8)	6 (6)	44 (10)
By hand movements or counting fingers*	42 (61) [48 - 72]	45 (76) [63 - 86]	26 (26) [18 - 36]	62 (61) [51 - 70]	81 (82) [73 - 89]	256 (60) [55 - 64]
It is not necessary to evaluate a patient's vision immediately after an Eylea injection	22 (32)	2 (3)	46 (46)	28 (27)	9 (9)	107 (25)
None of the above	0 (0)	0 (0)	4 (4)	2 (2)	1 (1)	7 (2)
I don't know	0 (0)	2 (3)	3 (3)	0 (0)	1 (1)	6 (1)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
An increase in intraocular pressure has been seen within 60 minutes after an injection with Eylea. (Q19)						
True*	60 (87) [77 - 94]	54 (92) [81 - 97]	76 (77) [67 - 85]	66 (65) [55 - 74]	83 (84) [75 - 90]	339 (79) [75 - 83]
False	6 (9)	2 (3)	11 (11)	19 (19)	5 (5)	43 (10)
I don't know	2 (3)	2 (3)	9 (9)	15 (15)	10 (10)	38 (9)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
What should physicians do in relation to the potential of increased intraocular pressure immediately following an Eylea injection? (Q20) Tick all that apply.						
Ensure that sterile equipment is available to perform paracentesis if necessary*	29 (42) [30 - 55]	48 (81) [69 - 90]	59 (60) [49 - 69]	68 (67) [57 - 76]	75 (76) [66 - 84]	279 (65) [60 - 70]
Undertake appropriate monitoring if increased intraocular pressure is suspected (e.g., check for perfusion of the optic nerve head or tonometry)*	32 (46) [34 - 59]	51 (86) [75 - 94]	74 (75) [65 - 83]	86 (84) [76 - 91]	91 (92) [85 - 96]	334 (78) [74 - 82]
Nothing needs to be done because increased ocular pressure is normal and never harmful	29 (42)	0 (0)	12 (12)	8 (8)	3 (3)	52 (12)
None of the above	1 (1)	1 (2)	0 (0)	0 (0)	0 (0)	2 (0)
I don't know	0 (0)	1 (2)	1 (1)	1 (1)	1 (1)	4 (1)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
Selected both of the correct responses	17 (25) [15 - 36]	43 (73) [60 - 84]	47 (47) [37 - 58]	61 (60) [50 - 69]	71 (72) [62 - 80]	239 (56) [51 - 61]
Selected at least one of the two correct responses	44 (64) [51 - 75]	56 (95) [86 - 99]	86 (87) [79 - 93]	93 (91) [84 - 96]	95 (96) [90 - 99]	374 (87) [84 - 90]
After the Eylea injection, patients should be instructed to report any symptoms suggestive of which of the following conditions? (Q21) Tick all that apply.						
Intraocular inflammation*	57 (83) [72 - 91]	56 (95) [86 - 99]	89 (90) [82 - 95]	82 (80) [71 - 88]	84 (85) [76 - 91]	368 (86) [82 - 89]
Drooping eyelid	16 (23)	19 (32)	34 (34)	19 (19)	28 (28)	116 (27)
Endophthalmitis*	67 (97) [90 - 100]	57 (97) [88 - 100]	84 (85) [76 - 91]	98 (96) [90 - 99]	95 (96) [90 - 99]	401 (94) [91 - 96]
None of the above	0 (0)	0 (0)	2 (2)	1 (1)	1 (1)	4 (1)
I don't know	0 (0)	1 (2)	1 (1)	1 (1)	0 (0)	3 (1)
No answer	1 (1)	1 (2)	3 (3)	2 (2)	1 (1)	8 (2)
Selected both of the correct responses	56 (81) [70 - 90]	56 (95) [86 - 99]	80 (81) [72 - 88]	82 (80) [71 - 88]	83 (84) [75 - 90]	357 (83) [80 - 87]
Selected at least one of the two correct responses	68 (99) [92 - 100]	57 (97) [88 - 100]	93 (94) [87 - 98]	98 (96) [90 - 99]	96 (97) [91 - 99]	412 (96) [94 - 98]

Table 3-5. Physician Knowledge: Side Effects, Overall and by Country

Question	France (N = 69) n (%) [95% CI]	Germany (N = 59) n (%) [95% CI]	Italy (N = 99) n (%) [95% CI]	Spain (N = 102) n (%) [95% CI]	UK (N = 99) n (%) [95% CI]	Overall (N = 428) n (%) [95% CI]
Which of the following signs or symptoms are known undesirable side effects of using Eylea? (Q22)						
Endophthalmitis						
Yes, this is an undesirable effect*	57 (83) [72 - 91]	56 (95) [86 - 99]	83 (84) [75 - 90]	94 (92) [85 - 97]	90 (91) [83 - 96]	380 (89) [85 - 92]
No, this is not an undesirable effect	10 (14)	1 (2)	10 (10)	5 (5)	7 (7)	33 (8)
I don't know	1 (1)	1 (2)	3 (3)	0 (0)	1 (1)	6 (1)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	1 (1)	9 (2)
Transient increased intraocular pressure						
Yes, this is an undesirable effect*	59 (86) [75 - 93]	55 (93) [84 - 98]	84 (85) [76 - 91]	87 (85) [77 - 92]	80 (81) [72 - 88]	365 (85) [82 - 89]
No, this is not an undesirable effect	9 (13)	3 (5)	11 (11)	10 (10)	18 (18)	51 (12)
I don't know	0 (0)	0 (0)	1 (1)	1 (1)	0 (0)	2 (0)
No answer	1 (1)	1 (2)	3 (3)	4 (4)	1 (1)	10 (2)
Fever						
Yes, this is an undesirable effect	8 (12)	15 (25)	18 (18)	15 (15)	24 (24)	80 (19)
No, this is not an undesirable effect*	49 (71) [59 - 81]	34 (58) [44 - 70]	59 (60) [49 - 69]	68 (67) [57 - 76]	60 (61) [50 - 70]	270 (63) [58 - 68]
I don't know	9 (13)	9 (15)	18 (18)	16 (16)	14 (14)	66 (15)
No answer	3 (4)	1 (2)	4 (4)	3 (3)	1 (1)	12 (3)
Cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities						
Yes, this is an undesirable effect*	46 (67) [54 - 78]	46 (78) [65 - 88]	70 (71) [61 - 79]	83 (81) [72 - 88]	87 (88) [80 - 94]	332 (78) [73 - 81]
No, this is not an undesirable effect	19 (28)	8 (14)	23 (23)	16 (16)	11 (11)	77 (18)
I don't know	3 (4)	4 (7)	3 (3)	0 (0)	0 (0)	10 (2)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	1 (1)	9 (2)
Tear or detachment of the retinal pigment epithelium						
Yes, this is an undesirable effect*	47 (68) [56 - 79]	52 (88) [77 - 95]	70 (71) [61 - 79]	88 (86) [78 - 92]	86 (87) [79 - 93]	343 (80) [76 - 84]
No, this is not an undesirable effect	18 (26)	4 (7)	21 (21)	10 (10)	9 (9)	62 (14)
I don't know	3 (4)	2 (3)	4 (4)	1 (1)	3 (3)	13 (3)
No answer	1 (1)	1 (2)	4 (4)	3 (3)	1 (1)	10 (2)
Headache						
Yes, this is an undesirable effect	25 (36)	26 (44)	27 (27)	23 (23)	35 (35)	136 (32)
No, this is not an undesirable effect*	31 (45) [33 - 57]	22 (37) [25 - 51]	47 (47) [37 - 58]	53 (52) [42 - 62]	49 (49) [39 - 60]	202 (47) [42 - 52]
I don't know	12 (17)	10 (17)	21 (21)	23 (23)	14 (14)	80 (19)
No answer	1 (1)	1 (2)	4 (4)	3 (3)	1 (1)	10 (2)

Table 4. Physician Receipt and Use of Aflibercept Educational Materials, Overall and by Country

Please indicate whether you have received and/or reviewed the following Eylea informational material. (Q23)	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Summary of Product Characteristics						
Have you received the material?						
Yes	62 (90)	56 (95)	82 (83)	82 (80)	91 (92)	373 (87)
No	6 (9)	2 (3)	14 (14)	16 (16)	5 (5)	43 (10)
No answer	1 (1)	1 (2)	3 (3)	4 (4)	3 (3)	12 (3)
Have you reviewed the material?						
Yes	50 (79)	49 (86)	77 (91)	71 (83)	84 (89)	331 (86)
No	11 (17)	2 (4)	2 (2)	8 (9)	6 (6)	29 (8)
No answer	2 (3)	6 (11)	6 (7)	7 (8)	4 (4)	25 (6)
Not applicable skip pattern (did not receive this material)	6	2	14	16	5	43
Eylea Prescriber Guide						
Have you received the material?						
Yes	57 (83)	56 (95)	71 (72)	65 (64)	81 (82)	330 (77)
No	10 (14)	2 (3)	25 (25)	33 (32)	16 (16)	86 (20)
No answer	2 (3)	1 (2)	3 (3)	4 (4)	2 (2)	12 (3)
Have you reviewed the material?						
Yes	47 (80)	45 (79)	65 (88)	57 (83)	70 (84)	284 (83)
No	10 (17)	5 (9)	3 (4)	6 (9)	10 (12)	34 (10)
No answer	2 (3)	7 (12)	6 (8)	6 (9)	3 (4)	24 (7)
Not applicable skip pattern (did not receive this material)	10	2	25	33	16	86
Intravitreal injection procedure video						
Have you received the material?						
Yes	39 (57)	33 (56)	50 (51)	37 (36)	53 (54)	212 (50)
No	28 (41)	24 (41)	46 (46)	61 (60)	44 (44)	203 (47)
No answer	2 (3)	2 (3)	3 (3)	4 (4)	2 (2)	13 (3)
Have you reviewed the material?						
Yes	20 (49)	20 (57)	38 (72)	30 (73)	35 (64)	143 (64)
No	18 (44)	9 (26)	8 (15)	4 (10)	17 (31)	56 (25)
No answer	3 (7)	6 (17)	7 (13)	7 (17)	3 (5)	26 (12)

Table 4. Physician Receipt and Use of Aflibercept Educational Materials, Overall and by Country

Please indicate whether you have received and/or reviewed the following Eylea informational material. (Q23)	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Not applicable skip pattern (did not receive this material)	28	24	46	61	44	203
Patient Booklet including a Patient Information Audio CD and the Patient Information Leaflet						
Have you received the material?						
Yes	43 (62)	38 (64)	45 (45)	31 (30)	73 (74)	230 (54)
No	23 (33)	20 (34)	50 (51)	67 (66)	24 (24)	184 (43)
No answer	3 (4)	1 (2)	4 (4)	4 (4)	2 (2)	14 (3)
Have you reviewed the material?						
Yes	28 (61)	19 (49)	34 (69)	25 (71)	52 (69)	158 (65)
No	15 (33)	14 (36)	9 (18)	4 (11)	20 (27)	62 (25)
No answer	3 (7)	6 (15)	6 (12)	6 (17)	3 (4)	24 (10)
Not applicable skip pattern (did not receive this material)	23	20	50	67	24	184

Table 5. Physician Ratings of Aflibercept Educational Materials, Overall and by Country

How helpful were these materials to you in treating and educating your patients? (Q24) [a]	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Summary of Product Characteristics						
1 - Not at all helpful	6 (10)	2 (4)	1 (1)	2 (2)	0 (0)	11 (3)
2	15 (24)	8 (14)	15 (18)	14 (16)	12 (13)	64 (17)
3	30 (48)	26 (46)	31 (36)	44 (51)	45 (48)	176 (46)
4 - Extremely helpful	11 (17)	20 (35)	35 (41)	22 (26)	34 (36)	122 (32)
No answer	1 (2)	1 (2)	3 (4)	4 (5)	3 (3)	12 (3)
Not applicable skip pattern (did not receive this material)	6	2	14	16	5	43
Eylea Prescriber Guide						
1 - Not at all helpful	6 (10)	2 (4)	3 (4)	3 (4)	0 (0)	14 (4)
2	16 (27)	8 (14)	11 (15)	10 (14)	12 (14)	57 (17)
3	22 (37)	29 (51)	20 (27)	34 (49)	40 (48)	145 (42)
4 - Extremely helpful	13 (22)	17 (30)	37 (50)	18 (26)	29 (35)	114 (33)
No answer	2 (3)	1 (2)	3 (4)	4 (6)	2 (2)	12 (4)
Not applicable skip pattern (did not receive this material)	10	2	25	33	16	86
Intravitreal injection procedure video						
1 - Not at all helpful	10 (24)	3 (9)	5 (9)	6 (15)	1 (2)	25 (11)
2	15 (37)	9 (26)	5 (9)	6 (15)	13 (24)	48 (21)
3	10 (24)	16 (46)	19 (36)	11 (27)	17 (31)	73 (32)
4 - Extremely helpful	4 (10)	5 (14)	21 (40)	14 (34)	22 (40)	66 (29)
No answer	2 (5)	2 (6)	3 (6)	4 (10)	2 (4)	13 (6)
Not applicable skip pattern (did not receive this material)	28	24	46	61	44	203
Patient Booklet						
1 - Not at all helpful	2 (4)	4 (10)	0 (0)	0 (0)	2 (3)	8 (3)
2	9 (20)	11 (28)	4 (8)	6 (17)	7 (9)	37 (15)
3	20 (43)	15 (38)	18 (37)	12 (34)	31 (41)	96 (39)
4 - Extremely helpful	11 (24)	8 (21)	23 (47)	13 (37)	33 (44)	88 (36)
No answer	4 (9)	1 (3)	4 (8)	4 (11)	2 (3)	15 (6)

Table 5. Physician Ratings of Aflibercept Educational Materials, Overall and by Country

How helpful were these materials to you in treating and educating your patients? (Q24) [a]	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Not applicable skip pattern (did not receive this material)	23	20	50	67	24	184
Patient Information Audio CD						
1 - Not at all helpful	4 (9)	6 (15)	4 (8)	4 (11)	4 (5)	22 (9)
2	13 (28)	11 (28)	9 (18)	10 (29)	11 (15)	54 (22)
3	16 (35)	14 (36)	15 (31)	9 (26)	34 (45)	88 (36)
4 - Extremely helpful	10 (22)	7 (18)	17 (35)	8 (23)	24 (32)	66 (27)
No answer	3 (7)	1 (3)	4 (8)	4 (11)	2 (3)	14 (6)
Not applicable skip pattern (did not receive this material)	23	20	50	67	24	184
Patient Information Leaflet						
1 - Not at all helpful	3 (7)	4 (10)	0 (0)	2 (6)	1 (1)	10 (4)
2	8 (17)	7 (18)	2 (4)	6 (17)	6 (8)	29 (12)
3	18 (39)	20 (51)	23 (47)	15 (43)	32 (43)	108 (44)
4 - Extremely helpful	14 (30)	7 (18)	20 (41)	8 (23)	34 (45)	83 (34)
No answer	3 (7)	1 (3)	4 (8)	4 (11)	2 (3)	14 (6)
Not applicable skip pattern (did not receive this material)	23	20	50	67	24	184

Table 6. Physician Use of Patient Booklet, Overall and by Country

Question	France (N = 69) n (%)	Germany (N = 59) n (%)	Italy (N = 99) n (%)	Spain (N = 102) n (%)	UK (N = 99) n (%)	Overall (N = 428) n (%)
Considering the patients under your care who are receiving Eylea injections, to how many did you provide a Patient Booklet? (Q26)						
All of my patients	15 (22)	10 (17)	27 (27)	19 (19)	46 (46)	117 (27)
Most of my patients	18 (26)	11 (19)	21 (21)	12 (12)	35 (35)	97 (23)
A few of my patients	20 (29)	22 (37)	28 (28)	24 (24)	10 (10)	104 (24)
None of my patients	15 (22)	15 (25)	20 (20)	44 (43)	6 (6)	100 (23)
No answer	1 (1)	1 (2)	3 (3)	3 (3)	2 (2)	10 (2)
When would you provide the Patient Booklet and discuss it with your patient? (Q27) Tick all that apply.						
Before the start of treatment with Eylea	51 (94)	40 (91)	74 (94)	54 (93)	89 (96)	308 (94)
When a patient has an Eylea-related adverse event	6 (11)	5 (11)	0 (0)	1 (2)	3 (3)	15 (5)
I do not reference the Patient Information Booklet	0 (0)	3 (7)	2 (3)	1 (2)	1 (1)	7 (2)
Other	0 (0)	1 (2)	1 (1)	1 (2)	1 (1)	4 (1)
No answer	1 (2)	1 (2)	3 (4)	3 (5)	2 (2)	10 (3)
Not applicable skip pattern (selected "None of my patients" for Q26)	15	15	20	44	6	100

Annex 6. Analysis Tables for Non-recruiting Physicians (Other Stratification Variables)

Tables

Table 3-1a. Physician Knowledge: Storage and Preparation by Experience with Eylea Prescriber Guide

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
Eylea is a suspension, which contains particulates and is cloudy				
Yes, this is true	46 (16)	3 (7)	12 (14)	1 (8)
No, this is not true*	209 (74)	40 (87)	59 (69)	9 (75)
I don't know	29 (10)	3 (7)	15 (17)	2 (17)
For the intravitreal injection, a 30-gauge x ½ inch injection needle should be used				
Yes, this is true*	256 (90)	41 (89)	73 (85)	12 (100)
No, this is not true	13 (5)	3 (7)	5 (6)	0 (0)
I don't know	15 (5)	2 (4)	8 (9)	0 (0)
Adequate anaesthesia and asepsis (e.g., use of povidone iodine) must be provided for the patient				
Yes, this is true*	280 (99)	44 (96)	82 (95)	11 (92)
No, this is not true	3 (1)	2 (4)	2 (2)	0 (0)
I don't know	1 (0)	0 (0)	2 (2)	1 (8)
Number of correct responses selected among the three Yes/No questions listed above				
0	1 (0)	0 (0)	2 (2)	0 (0)
1	10 (4)	3 (7)	8 (9)	1 (8)
2	84 (30)	7 (15)	22 (26)	2 (17)
3	189 (67)	36 (78)	54 (63)	9 (75)

Table 3-1a. Physician Knowledge: Storage and Preparation by Experience with Eylea Prescriber Guide

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
The next three questions were only asked of those physicians who indicated they use the vial				
Not applicable skip pattern	110	21	36	8
The vial of Eylea is reusable between patients and can be used for multiple injections				
Yes, this is true	17 (10)	3 (12)	11 (22)	1 (25)
No, this is not true*	147 (84)	22 (88)	36 (72)	3 (75)
I don't know	7 (4)	0 (0)	3 (6)	0 (0)
No answer	3 (2)	0 (0)	0 (0)	0 (0)
The vial of Eylea must be stored in the refrigerator (2°C to 8°C)				
Yes, this is true*	151 (87)	20 (80)	37 (74)	4 (100)
No, this is not true	9 (5)	3 (12)	5 (10)	0 (0)
I don't know	13 (7)	2 (8)	8 (16)	0 (0)
No answer	1 (1)	0 (0)	0 (0)	0 (0)
Prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours				
Yes, this is true	60 (34)	5 (20)	8 (16)	0 (0)
No, this is not true*	66 (38)	14 (56)	23 (46)	2 (50)
I don't know	47 (27)	6 (24)	19 (38)	2 (50)
No answer	1 (1)	0 (0)	0 (0)	0 (0)
Number of correct responses selected among the three Yes/No questions listed above				
0	3 (2)	0 (0)	4 (8)	0 (0)
1	36 (21)	3 (12)	10 (20)	1 (25)
2	77 (44)	13 (52)	22 (44)	1 (25)
3	58 (33)	9 (36)	14 (28)	2 (50)

Table 3-2a. Physician Knowledge: Dosing and Monitoring, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
What is the recommended dose for Eylea? (Q2)				
12.5 microlitres (0.5 mg)	41 (14)	7 (15)	18 (21)	1 (8)
50 microlitres (2 mg)*	221 (78)	31 (67)	54 (63)	7 (58)
90 microlitres (3.6 mg)	2 (1)	3 (7)	0 (0)	0 (0)
100 microlitres (4 mg)	11 (4)	2 (4)	3 (3)	0 (0)
I don't know	9 (3)	3 (7)	11 (13)	1 (8)
No answer	0 (0)	0 (0)	0 (0)	3 (25)
For each of the following statements related to the Eylea dosing and monitoring recommendations for the treatment of wAMD, please indicate if the statement is true, not true, or if you do not know. (Q3)				
Not applicable skip pattern (did not tick wAMD in screener question 2)	6	2	4	0
During the first 12 months, treatment is initiated with one injection per month for three consecutive doses, followed by one injection every 2 months.				
Yes, this is true*	266 (96)	38 (86)	69 (84)	5 (42)
No, this is not true	11 (4)	5 (11)	10 (12)	0 (0)
I don't know	1 (0)	0 (0)	3 (4)	1 (8)
No answer	0 (0)	1 (2)	0 (0)	6 (50)

Table 3-2a. Physician Knowledge: Dosing and Monitoring, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
During the first 12 months, there is no requirement for monitoring between injections.				
Yes, this is true*	81 (29)	16 (36)	20 (24)	0 (0)
No, this is not true	192 (69)	28 (64)	59 (72)	4 (33)
I don't know	4 (1)	0 (0)	3 (4)	1 (8)
No answer	1 (0)	0 (0)	0 (0)	7 (58)
After the first 12 months, the treatment interval may be extended based on visual and anatomical outcomes.				
Yes, this is true*	273 (98)	41 (93)	72 (88)	4 (33)
No, this is not true	4 (1)	3 (7)	5 (6)	1 (8)
I don't know	1 (0)	0 (0)	4 (5)	1 (8)
No answer	0 (0)	0 (0)	1 (1)	6 (50)
After the first 12 months, the schedule for monitoring should be determined by the treating physician and may be more frequent than the schedule of injections.				
Yes, this is true*	244 (88)	35 (80)	57 (70)	5 (42)
No, this is not true	26 (9)	5 (11)	13 (16)	0 (0)
I don't know	8 (3)	4 (9)	11 (13)	1 (8)
No answer	0 (0)	0 (0)	1 (1)	6 (50)
Number of correct responses selected among the four Yes/No questions listed above				
0	0 (0)	0 (0)	2 (2)	7 (58)
1	5 (2)	3 (7)	7 (9)	0 (0)
2	29 (10)	7 (16)	23 (28)	1 (8)
3	175 (63)	23 (52)	35 (43)	4 (33)
4	69 (25)	11 (25)	15 (18)	0 (0)

Table 3-2a. Physician Knowledge: Dosing and Monitoring, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
For each of the following statements related to the Eylea dosing recommendations for the treatment of macular oedema secondary to CRVO or BRVO, please indicate if the statement is true, not true, or if you do not know. (Q4)				
Not applicable skip pattern (did not tick CRVO or BRVO in screener question 2)	67	16	33	5
After the initial injection, treatment is given monthly.				
Yes, this is true*	138 (64)	19 (63)	30 (57)	1 (14)
No, this is not true	72 (33)	11 (37)	21 (40)	3 (43)
I don't know	7 (3)	0 (0)	2 (4)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	3 (43)
The interval between two doses should not be shorter than 2 months.				
Yes, this is true	53 (24)	9 (30)	14 (26)	2 (29)
No, this is not true*	152 (70)	20 (67)	38 (72)	2 (29)
I don't know	12 (6)	1 (3)	1 (2)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	3 (43)
If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued.				
Yes, this is true*	177 (82)	27 (90)	44 (83)	2 (29)
No, this is not true	30 (14)	3 (10)	8 (15)	1 (14)
I don't know	10 (5)	0 (0)	1 (2)	1 (14)
No answer	0 (0)	0 (0)	0 (0)	3 (43)

Table 3-2a. Physician Knowledge: Dosing and Monitoring, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity.				
Yes, this is true*	178 (82)	24 (80)	38 (72)	3 (43)
No, this is not true	34 (16)	5 (17)	14 (26)	1 (14)
I don't know	5 (2)	1 (3)	1 (2)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	3 (43)
Number of correct responses selected among the four Yes/No questions listed above				
0	2 (1)	0 (0)	2 (4)	3 (43)
1	16 (7)	1 (3)	3 (6)	1 (14)
2	37 (17)	9 (30)	12 (23)	2 (29)
3	93 (43)	9 (30)	21 (40)	1 (14)
4	69 (32)	11 (37)	15 (28)	0 (0)
For each of the following statements related to the Eylea dosing recommendations for the treatment of DME, please indicate if the statement is true, not true, or if you do not know. (Q5)				
Not applicable skip pattern (did not tick DME in screener question 2)	50	12	24	2
Eylea treatment is initiated with one injection per month for five consecutive doses.				
Yes, this is true*	170 (73)	22 (65)	45 (73)	3 (30)
No, this is not true	59 (25)	10 (29)	16 (26)	1 (10)
I don't know	5 (2)	2 (6)	1 (2)	1 (10)
No answer	0 (0)	0 (0)	0 (0)	5 (50)

Table 3-2a. Physician Knowledge: Dosing and Monitoring, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
After the first 5 months, Eylea treatment is followed by one injection every 2 months.				
Yes, this is true*	178 (76)	22 (65)	43 (69)	4 (40)
No, this is not true	47 (20)	9 (26)	16 (26)	0 (0)
I don't know	9 (4)	3 (9)	2 (3)	1 (10)
No answer	0 (0)	0 (0)	1 (2)	5 (50)
During the first 12 months, there is no requirement for monitoring between injections.				
Yes, this is true*	58 (25)	10 (29)	19 (31)	0 (0)
No, this is not true	172 (74)	23 (68)	41 (66)	4 (40)
I don't know	4 (2)	1 (3)	2 (3)	1 (10)
No answer	0 (0)	0 (0)	0 (0)	5 (50)
Number of correct responses selected among the three Yes/No questions listed above				
0	36 (15)	9 (26)	8 (13)	6 (60)
1	40 (17)	6 (18)	12 (19)	1 (10)
2	108 (46)	9 (26)	31 (50)	3 (30)
3	50 (21)	10 (29)	11 (18)	0 (0)
The Eylea vial contains more than the recommended dose of Eylea and excess volume should be expelled before injecting. (Q8)				
True*	156 (90)	21 (84)	42 (84)	2 (50)
False	13 (7)	4 (16)	5 (10)	0 (0)
I don't know	5 (3)	0 (0)	3 (6)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	2 (50)
Not applicable skip pattern	110	21	36	8

Table 3-2a. Physician Knowledge: Dosing and Monitoring, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
After removing all of the drug from the Eylea vial with a syringe, the plunger of the syringe should be depressed until the tip aligns with the line that marks which number of millilitres (ml) on the syringe? (Q9)				
0.05 ml*	125 (72)	14 (56)	29 (58)	2 (50)
0.1 ml	11 (6)	2 (8)	5 (10)	0 (0)
0.15 ml	2 (1)	0 (0)	0 (0)	0 (0)
0.2 ml	10 (6)	2 (8)	2 (4)	0 (0)
0.5 ml	19 (11)	6 (24)	8 (16)	0 (0)
I don't know	7 (4)	1 (4)	6 (12)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	2 (50)
Not applicable skip pattern	110	21	36	8

Table 3-3a. Physician Knowledge: Safe Use, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
What should you do to prepare the patient before the start of treatment with Eylea? (Q10) Tick all that apply.				
Provide the Patient Booklet which includes a Patient Information Audio CD and Patient Information Leaflet*	192 (68)	26 (57)	50 (58)	2 (17)
Explain the implications of anti-VEGF treatment*	273 (96)	44 (96)	81 (94)	4 (33)
Inform the patient to report any signs and symptoms potentially associated with serious adverse events and provide information on when to seek medical attention*	275 (97)	41 (89)	79 (92)	3 (25)
None of the above	1 (0)	0 (0)	0 (0)	0 (0)
I don't know	1 (0)	0 (0)	1 (1)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
Selected all three of the correct responses	190 (67)	24 (52)	48 (56)	2 (17)
Selected at least two of the three correct responses	268 (94)	41 (89)	77 (90)	3 (25)
Selected at least one of the three correct responses	282 (99)	46 (100)	85 (99)	4 (33)

Table 3-3a. Physician Knowledge: Safe Use, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
Eylea is contraindicated in which of the following patients? (Q11) Tick all that apply.				
Patients with a known hypersensitivity to Eylea or to any of the excipients (e.g., non-active ingredients)*	277 (98)	45 (98)	80 (93)	3 (25)
Patients with active or suspected ocular or periocular infection*	269 (95)	41 (89)	82 (95)	4 (33)
Patients with high blood pressure	31 (11)	6 (13)	7 (8)	1 (8)
Patients with active severe intraocular inflammation*	250 (88)	39 (85)	72 (84)	2 (17)
None of the above	1 (0)	0 (0)	0 (0)	0 (0)
I don't know	2 (1)	0 (0)	1 (1)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
Selected all three of the correct responses	241 (85)	36 (78)	70 (81)	2 (17)
Selected at least two of the three correct responses	274 (96)	43 (93)	79 (92)	3 (25)
Selected at least one of the three correct responses	281 (99)	46 (100)	85 (99)	4 (33)

Table 3-3a. Physician Knowledge: Safe Use, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
What is the recommended use of Eylea in women of childbearing potential? (Q12) Tick all that apply.				
Women of childbearing potential must use effective contraception during treatment and for at least 1 month after the last Eylea injection	26 (9)	4 (9)	8 (9)	0 (0)
Women of childbearing potential must use effective contraception during treatment and for at least 3 months after the last Eylea injection*	147 (52)	20 (43)	37 (43)	1 (8)
Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus*	176 (62)	30 (65)	46 (53)	2 (17)
Eylea should never be used in pregnancy	82 (29)	8 (17)	25 (29)	0 (0)
I don't know	25 (9)	7 (15)	14 (16)	1 (8)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
Selected both of the correct responses	98 (35)	14 (30)	25 (29)	0 (0)
Selected at least one of the two correct responses	225 (79)	36 (78)	58 (67)	3 (25)

Table 3-4a. Physician Knowledge: Injection Procedure, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
Should topical anaesthesia be used prior to the Eylea injection? (Q13)				
Yes, this is true*	274 (96)	42 (91)	82 (95)	4 (33)
No, this is not true	9 (3)	3 (7)	2 (2)	0 (0)
I don't know	1 (0)	1 (2)	2 (2)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
A disinfectant (e.g., povidone iodine solution) should be applied to the periocular skin, eyelid, and ocular surface. (Q14)				
True*	278 (98)	44 (96)	83 (97)	4 (33)
False	4 (1)	2 (4)	1 (1)	0 (0)
I don't know	2 (1)	0 (0)	2 (2)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
After the disinfectant is applied, which of the following steps should be taken prior to marking the scleral injection site? (Q15) Tick all that apply.				
Cover the eye with a sterile drape*	251 (88)	42 (91)	69 (80)	4 (33)
Insert a sterile lid speculum*	261 (92)	41 (89)	73 (85)	3 (25)
Dilate the eye	84 (30)	13 (28)	21 (24)	0 (0)
I don't know	1 (0)	0 (0)	1 (1)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
Selected both of the correct responses	231 (81)	38 (83)	58 (67)	3 (25)
Selected at least one of the two correct responses	281 (99)	45 (98)	84 (98)	4 (33)

Table 3-4a. Physician Knowledge: Injection Procedure, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
In preparation for the Eylea injection, the eye should be marked at which of the following positions: (Q16)				
At a distance 3.0 to 3.5 mm posterior to the limbus	27 (10)	11 (24)	4 (5)	0 (0)
At a distance 3.5 to 4.0 mm posterior to the limbus*	243 (86)	34 (74)	76 (88)	4 (33)
At a distance 4.0 to 4.5 mm posterior to the limbus	8 (3)	1 (2)	2 (2)	0 (0)
I don't know	6 (2)	0 (0)	4 (5)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
How should the injection needle be inserted into the eye? (Q17)				
Into the vitreous cavity, aiming to the anterior part of the globe to avoid injuring the retina	15 (5)	3 (7)	3 (3)	2 (17)
Into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe*	257 (90)	41 (89)	75 (87)	2 (17)
Into the vitreous cavity, aiming towards the posterior surface of the lens	6 (2)	2 (4)	4 (5)	0 (0)
Under the conjunctiva	1 (0)	0 (0)	1 (1)	0 (0)
I don't know	5 (2)	0 (0)	3 (3)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)

Table 3-5a. Physician Knowledge: Side Effects, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
How should physicians evaluate a patient's vision immediately after an Eylea injection? (Q18)				
Using a standard eye chart (e.g., Snellen, Notation Monoyer, Letter Score, ETDRS, Decimal)	28 (10)	5 (11)	10 (12)	1 (8)
By hand movements or counting fingers*	183 (64)	30 (65)	40 (47)	3 (25)
It is not necessary to evaluate a patient's vision immediately after an Eylea injection	66 (23)	11 (24)	30 (35)	0 (0)
None of the above	4 (1)	0 (0)	3 (3)	0 (0)
I don't know	3 (1)	0 (0)	3 (3)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
An increase in intraocular pressure has been seen within 60 minutes after an injection with Eylea. (Q19)				
True*	236 (83)	41 (89)	59 (69)	3 (25)
False	28 (10)	2 (4)	13 (15)	0 (0)
I don't know	20 (7)	3 (7)	14 (16)	1 (8)
No answer	0 (0)	0 (0)	0 (0)	8 (67)

Table 3-5a. Physician Knowledge: Side Effects, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
What should physicians do in relation to the potential of increased intraocular pressure immediately following an Eylea injection? (Q20) Tick all that apply.				
Ensure that sterile equipment is available to perform paracentesis if necessary*	188 (66)	37 (80)	52 (60)	2 (17)
Undertake appropriate monitoring if increased intraocular pressure is suspected (e.g., check for perfusion of the optic nerve head or tonometry)*	232 (82)	30 (65)	70 (81)	2 (17)
Nothing needs to be done because increased ocular pressure is normal and never harmful	35 (12)	8 (17)	8 (9)	1 (8)
None of the above	2 (1)	0 (0)	0 (0)	0 (0)
I don't know	2 (1)	0 (0)	1 (1)	1 (8)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
Selected both of the correct responses	167 (59)	27 (59)	43 (50)	2 (17)
Selected at least one of the two correct responses	253 (89)	40 (87)	79 (92)	2 (17)
After the Eylea injection, patients should be instructed to report any symptoms suggestive of which of the following conditions? (Q21) Tick all that apply.				
Intraocular inflammation*	253 (89)	40 (87)	72 (84)	3 (25)
Drooping eyelid	81 (29)	12 (26)	21 (24)	2 (17)
Endophthalmitis*	272 (96)	45 (98)	82 (95)	2 (17)
None of the above	3 (1)	0 (0)	1 (1)	0 (0)
I don't know	1 (0)	0 (0)	1 (1)	1 (8)
No answer	0 (0)	0 (0)	0 (0)	8 (67)
Selected both of the correct responses	245 (86)	40 (87)	70 (81)	2 (17)
Selected at least one of the two correct responses	280 (99)	45 (98)	84 (98)	3 (25)

Table 3-5a. Physician Knowledge: Side Effects, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
Which of the following signs or symptoms are known undesirable side effects of using Eylea? (Q22)				
Endophthalmitis				
Yes, this is true*	255 (90)	42 (91)	80 (93)	3 (25)
No, this is not true	24 (8)	4 (9)	5 (6)	0 (0)
I don't know	5 (2)	0 (0)	1 (1)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	9 (75)
Transient increased intraocular pressure				
Yes, this is true*	250 (88)	40 (87)	72 (84)	3 (25)
No, this is not true	33 (12)	6 (13)	12 (14)	0 (0)
I don't know	1 (0)	0 (0)	1 (1)	0 (0)
No answer	0 (0)	0 (0)	1 (1)	9 (75)
Fever				
Yes, this is true	49 (17)	11 (24)	18 (21)	2 (17)
No, this is not true*	186 (65)	28 (61)	55 (64)	1 (8)
I don't know	48 (17)	6 (13)	12 (14)	0 (0)
No answer	1 (0)	1 (2)	1 (1)	9 (75)
Cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities				
Yes, this is true*	226 (80)	37 (80)	66 (77)	3 (25)
No, this is not true	49 (17)	9 (20)	19 (22)	0 (0)
I don't know	9 (3)	0 (0)	1 (1)	0 (0)
No answer	0 (0)	0 (0)	0 (0)	9 (75)

Table 3-5a. Physician Knowledge: Side Effects, by Experience with Eylea Prescriber Guide

Question	Read (N = 284) n (%)	Received, Did Not Read (N = 46) n (%)	Did Not Receive (N = 86) n (%)	Skipped (N = 12) n (%)
Tear or detachment of the retinal pigment epithelium				
Yes, this is true*	236 (83)	37 (80)	69 (80)	1 (8)
No, this is not true	38 (13)	7 (15)	15 (17)	2 (17)
I don't know	10 (4)	1 (2)	2 (2)	0 (0)
No answer	0 (0)	1 (2)	0 (0)	9 (75)
Headache				
Yes, this is true	88 (31)	20 (43)	28 (33)	0 (0)
No, this is not true*	139 (49)	17 (37)	45 (52)	1 (8)
I don't know	57 (20)	8 (17)	13 (15)	2 (17)
No answer	0 (0)	1 (2)	0 (0)	9 (75)

Tables

Table 3-1b. Physician Knowledge: Storage and Preparation by Who Has the Primary Responsibility of Preparing Eylea Injection

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	I am responsible (N = 233) n (%)	A specialized nurse (N = 124) n (%)	Pharmacy (N = 62) n (%)	Laboratory (N = 3) n (%)	Other (N = 6) n (%)
Eylea is a suspension, which contains particulates and is cloudy					
Yes, this is true	41 (18)	17 (14)	4 (6)	0 (0)	0 (0)
No, this is not true*	175 (75)	89 (72)	48 (77)	2 (67)	3 (50)
I don't know	17 (7)	18 (15)	10 (16)	1 (33)	3 (50)
For the intravitreal injection, a 30-gauge x ½ inch injection needle should be used					
Yes, this is true*	213 (91)	102 (82)	60 (97)	2 (67)	5 (83)
No, this is not true	11 (5)	7 (6)	2 (3)	1 (33)	0 (0)
I don't know	9 (4)	15 (12)	0 (0)	0 (0)	1 (17)
Adequate anaesthesia and asepsis (e.g., use of povidone iodine) must be provided for the patient					
Yes, this is true*	227 (97)	120 (97)	62 (100)	2 (67)	6 (100)
No, this is not true	4 (2)	2 (2)	0 (0)	1 (33)	0 (0)
I don't know	2 (1)	2 (2)	0 (0)	0 (0)	0 (0)
Number of correct responses selected among the three Yes/No questions listed above					
0	0 (0)	3 (2)	0 (0)	0 (0)	0 (0)
1	12 (5)	8 (6)	0 (0)	1 (33)	1 (17)
2	60 (26)	36 (29)	16 (26)	1 (33)	2 (33)
3	161 (69)	77 (62)	46 (74)	1 (33)	3 (50)

Table 3-1b. Physician Knowledge: Storage and Preparation by Who Has the Primary Responsibility of Preparing Eylea Injection

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	I am responsible (N = 233) n (%)	A specialized nurse (N = 124) n (%)	Pharmacy (N = 62) n (%)	Laboratory (N = 3) n (%)	Other (N = 6) n (%)
The next three questions were only asked of those physicians who indicated they use the vial					
Not applicable skip pattern	74	72	22	3	4
The vial of Eylea is reusable between patients and can be used for multiple injections					
Yes, this is true	12 (8)	1 (2)	19 (48)	0 (0)	0 (0)
No, this is not true*	140 (88)	48 (92)	18 (45)	0 (0)	2 (100)
I don't know	5 (3)	3 (6)	2 (5)	0 (0)	0 (0)
No answer	2 (1)	0 (0)	1 (3)	0 (0)	0 (0)
The vial of Eylea must be stored in the refrigerator (2°C to 8°C)					
Yes, this is true*	130 (82)	46 (88)	34 (85)	0 (0)	2 (100)
No, this is not true	15 (9)	0 (0)	2 (5)	0 (0)	0 (0)
I don't know	13 (8)	6 (12)	4 (10)	0 (0)	0 (0)
No answer	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours					
Yes, this is true	51 (32)	14 (27)	7 (18)	0 (0)	1 (50)
No, this is not true*	63 (40)	23 (44)	19 (48)	0 (0)	0 (0)
I don't know	44 (28)	15 (29)	14 (35)	0 (0)	1 (50)
No answer	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Number of correct responses selected among the three Yes/No questions listed above					
0	1 (1)	2 (4)	4 (10)	0 (0)	0 (0)
1	35 (22)	5 (10)	10 (25)	0 (0)	0 (0)
2	71 (45)	23 (44)	17 (43)	0 (0)	2 (100)
3	52 (33)	22 (42)	9 (23)	0 (0)	0 (0)

Annex 7. Analysis Tables for Patients (Overall and by Country)

Tables

Table 1. Patient Characteristics, Overall and by Country

Question	France (N = 114) n (%)	Germany (N = 158) n (%)	Italy (N = 168) n (%)	Spain (N = 169) n (%)	UK (N = 164) n (%)	Overall (N = 773) n (%)
How old are you? (Q10)						
18 - 25 years	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
26 - 35 years	0 (0)	1 (1)	1 (1)	1 (1)	0 (0)	3 (0)
36 - 45 years	0 (0)	1 (1)	0 (0)	1 (1)	2 (1)	4 (1)
46 - 55 years	8 (7)	7 (4)	3 (2)	10 (6)	6 (4)	34 (4)
56 - 65 years	12 (11)	24 (15)	23 (14)	28 (17)	20 (12)	107 (14)
66 - 75 years	31 (27)	51 (32)	56 (33)	49 (29)	53 (32)	240 (31)
76 - 85 years	48 (42)	56 (35)	69 (41)	60 (36)	62 (38)	295 (38)
86 years or older	15 (13)	18 (11)	16 (10)	20 (12)	21 (13)	90 (12)
Sex (collected on patient screener recruitment form)						
Female	69 (61)	85 (54)	86 (51)	86 (51)	91 (55)	417 (54)
Male	45 (39)	73 (46)	82 (49)	83 (49)	73 (45)	356 (46)
What is the highest level of education you have completed? (Q11) (Please choose one answer only.)						
No university (primary school, secondary school, university or professional preparation)	81 (71)	121 (77)	150 (89)	141 (83)	138 (84)	631 (82)
Undergraduate and/or post-graduate university	33 (29)	33 (21)	18 (11)	24 (14)	25 (15)	133 (17)
No answer	0 (0)	4 (3)	0 (0)	4 (2)	1 (1)	9 (1)
We are interested in knowing if you receive any help from anyone other than your doctor or nurse (e.g., a family member, friend, or caregiver) in relation to your eye treatment. (Q12)						
How often do you need to have someone other than your doctor or nurse READ information materials to you?						
None of the time	84 (74)	116 (73)	103 (61)	96 (57)	115 (70)	514 (66)
Some of the time	12 (11)	23 (15)	36 (21)	23 (14)	26 (16)	120 (16)
Most of the time	6 (5)	5 (3)	12 (7)	18 (11)	10 (6)	51 (7)
All of the time	10 (9)	8 (5)	17 (10)	28 (17)	11 (7)	74 (10)
I don't know	2 (2)	6 (4)	0 (0)	4 (2)	2 (1)	14 (2)

Table 1. Patient Characteristics, Overall and by Country

Question	France (N = 114) n (%)	Germany (N = 158) n (%)	Italy (N = 168) n (%)	Spain (N = 169) n (%)	UK (N = 164) n (%)	Overall (N = 773) n (%)
How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you?						
None of the time	87 (76)	109 (69)	107 (64)	91 (54)	118 (72)	512 (66)
Some of the time	14 (12)	34 (22)	36 (21)	35 (21)	31 (19)	150 (19)
Most of the time	8 (7)	3 (2)	10 (6)	14 (8)	6 (4)	41 (5)
All of the time	4 (4)	6 (4)	15 (9)	25 (15)	8 (5)	58 (8)
I don't know	1 (1)	6 (4)	0 (0)	4 (2)	1 (1)	12 (2)
How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you?						
None of the time	91 (80)	127 (80)	121 (72)	125 (74)	144 (88)	608 (79)
Some of the time	11 (10)	18 (11)	30 (18)	21 (12)	14 (9)	94 (12)
Most of the time	6 (5)	3 (2)	7 (4)	9 (5)	4 (2)	29 (4)
All of the time	5 (4)	4 (3)	10 (6)	12 (7)	1 (1)	32 (4)
I don't know	1 (1)	6 (4)	0 (0)	2 (1)	1 (1)	10 (1)

Table 2. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, Overall and by Country

Question	France (N = 114) n (%) [95% CI]	Germany (N = 158) n (%) [95% CI]	Italy (N = 168) n (%) [95% CI]	Spain (N = 169) n (%) [95% CI]	UK (N = 164) n (%) [95% CI]	Overall (N = 773) n (%) [95% CI]
Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Q1)						
Any current eye problems (for example, infection, pain or redness in the eye)						
Yes*	100 (88) [80 - 93]	150 (95) [90 - 98]	158 (94) [89 - 97]	147 (87) [81 - 92]	155 (95) [90 - 97]	710 (92) [90 - 94]
No	10 (9)	7 (4)	10 (6)	15 (9)	8 (5)	50 (6)
I don't know	4 (4)	1 (1)	0 (0)	7 (4)	1 (1)	13 (2)
Any allergies to medications (for example, iodine or painkillers)						
Yes*	93 (82) [73 - 88]	143 (91) [85 - 95]	153 (91) [86 - 95]	157 (93) [88 - 96]	149 (91) [85 - 95]	695 (90) [88 - 92]
No	17 (15)	10 (6)	10 (6)	8 (5)	11 (7)	56 (7)
I don't know	4 (4)	5 (3)	5 (3)	4 (2)	4 (2)	22 (3)
Any problems with eye injections in the past						
Yes*	99 (87) [79 - 92]	140 (89) [83 - 93]	154 (92) [86 - 95]	154 (91) [86 - 95]	143 (87) [81 - 92]	690 (89) [87 - 91]
No	13 (11)	12 (8)	12 (7)	6 (4)	18 (11)	61 (8)
I don't know	2 (2)	5 (3)	2 (1)	9 (5)	3 (2)	21 (3)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	1 (0)
If you have glaucoma or have had issues with feeling of high pressure in the eye in the past						
Yes*	90 (79) [70 - 86]	142 (90) [84 - 94]	137 (82) [75 - 87]	154 (91) [86 - 95]	143 (87) [81 - 92]	666 (86) [84 - 89]
No	18 (16)	7 (4)	21 (13)	2 (1)	14 (9)	62 (8)
I don't know	6 (5)	9 (6)	10 (6)	13 (8)	6 (4)	44 (6)
No answer	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (0)
If you see flashes of light						
Yes*	92 (81) [72 - 87]	144 (91) [86 - 95]	149 (89) [83 - 93]	155 (92) [86 - 95]	137 (84) [77 - 89]	677 (88) [85 - 90]
No	19 (17)	7 (4)	14 (8)	8 (5)	16 (10)	64 (8)
I don't know	3 (3)	7 (4)	5 (3)	6 (4)	10 (6)	31 (4)
No answer	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (0)
If you see moving spots (known as floaters) in your eye						
Yes*	95 (83) [75 - 90]	149 (94) [89 - 97]	153 (91) [86 - 95]	148 (88) [82 - 92]	128 (78) [71 - 84]	673 (87) [84 - 89]
No	16 (14)	6 (4)	11 (7)	10 (6)	30 (18)	73 (9)
I don't know	3 (3)	3 (2)	4 (2)	11 (7)	5 (3)	26 (3)
No answer	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (0)
Any medications that you have used						
Yes*	87 (76) [67 - 84]	143 (91) [85 - 95]	148 (88) [82 - 93]	137 (81) [74 - 87]	140 (85) [79 - 90]	655 (85) [82 - 87]
No	19 (17)	8 (5)	9 (5)	19 (11)	19 (12)	74 (10)
I don't know	8 (7)	7 (4)	11 (7)	13 (8)	5 (3)	44 (6)

Table 2. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, Overall and by Country

Question	France (N = 114) n (%) [95% CI]	Germany (N = 158) n (%) [95% CI]	Italy (N = 168) n (%) [95% CI]	Spain (N = 169) n (%) [95% CI]	UK (N = 164) n (%) [95% CI]	Overall (N = 773) n (%) [95% CI]
If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection						
Yes*	95 (83) [75 - 90]	141 (89) [83 - 94]	149 (89) [83 - 93]	153 (91) [85 - 94]	144 (88) [82 - 92]	682 (88) [86 - 90]
No	17 (15)	14 (9)	15 (9)	5 (3)	16 (10)	67 (9)
I don't know	2 (2)	3 (2)	4 (2)	11 (7)	4 (2)	24 (3)
If you are pregnant, are planning to become pregnant, or are breastfeeding						
Yes*	46 (40) [31 - 50]	83 (53) [44 - 61]	86 (51) [43 - 59]	102 (60) [53 - 68]	82 (50) [42 - 58]	399 (52) [48 - 55]
No	48 (42)	49 (31)	47 (28)	26 (15)	50 (30)	220 (28)
I don't know	17 (15)	20 (13)	35 (21)	39 (23)	29 (18)	140 (18)
No answer	3 (3)	6 (4)	0 (0)	2 (1)	3 (2)	14 (2)
Number of correct responses selected among the nine Yes/No questions listed above						
0	1 (1)	0 (0)	0 (0)	3 (2)	1 (1)	5 (1)
1	2 (2)	2 (1)	1 (1)	0 (0)	2 (1)	7 (1)
2	6 (5)	3 (2)	1 (1)	1 (1)	0 (0)	11 (1)
3	4 (4)	1 (1)	7 (4)	1 (1)	1 (1)	14 (2)
4	5 (4)	3 (2)	2 (1)	5 (3)	9 (5)	24 (3)
5	5 (4)	4 (3)	11 (7)	4 (2)	9 (5)	33 (4)
6	6 (5)	10 (6)	13 (8)	11 (7)	18 (11)	58 (8)
7	23 (20)	15 (9)	17 (10)	23 (14)	22 (13)	100 (13)
8	29 (25)	53 (34)	41 (24)	54 (32)	45 (27)	222 (29)
9	33 (29)	67 (42)	75 (45)	67 (40)	57 (35)	299 (39)

Table 3. Patient Knowledge: Possible Side Effects, Overall and by Country

Question	France (N = 114) n (%) [95% CI]	Germany (N = 158) n (%) [95% CI]	Italy (N = 168) n (%) [95% CI]	Spain (N = 169) n (%) [95% CI]	UK (N = 164) n (%) [95% CI]	Overall (N = 773) n (%) [95% CI]
We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] possible side effect of Eylea? (Q2)						
...a red or bloodshot eye						
Yes*	75 (66) [56 - 74]	101 (64) [56 - 71]	135 (80) [74 - 86]	121 (72) [64 - 78]	111 (68) [60 - 75]	543 (70) [67 - 73]
No	32 (28)	34 (22)	19 (11)	25 (15)	34 (21)	144 (19)
I don't know	7 (6)	23 (15)	14 (8)	23 (14)	19 (12)	86 (11)
...nausea and vomiting (feeling or being sick)						
Yes	24 (21)	43 (27)	65 (39)	54 (32)	42 (26)	228 (29)
No*	70 (61) [52 - 70]	83 (53) [44 - 61]	77 (46) [38 - 54]	77 (46) [38 - 53]	104 (63) [56 - 71]	411 (53) [50 - 57]
I don't know	20 (18)	32 (20)	26 (15)	38 (22)	18 (11)	134 (17)
...eye pain						
Yes*	78 (68) [59 - 77]	107 (68) [60 - 75]	129 (77) [70 - 83]	129 (76) [69 - 83]	126 (77) [70 - 83]	569 (74) [70 - 77]
No	33 (29)	40 (25)	32 (19)	26 (15)	29 (18)	160 (21)
I don't know	3 (3)	11 (7)	7 (4)	14 (8)	9 (5)	44 (6)
...detachment of the gel-like substance inside the eye from the retina						
Yes*	33 (29) [21 - 38]	67 (42) [35 - 51]	82 (49) [41 - 57]	91 (54) [46 - 62]	52 (32) [25 - 39]	325 (42) [39 - 46]
No	45 (39)	41 (26)	36 (21)	36 (21)	60 (37)	218 (28)
I don't know	36 (32)	50 (32)	50 (30)	42 (25)	52 (32)	230 (30)
...seeing halos around lights						
Yes*	52 (46) [36 - 55]	NA	119 (71) [63 - 78]	93 (55) [47 - 63]	85 (52) [44 - 60]	349 (57) [53 - 61]
No	43 (38)	NA	30 (18)	39 (23)	58 (35)	170 (28)
I don't know	19 (17)	NA	19 (11)	37 (22)	21 (13)	96 (16)
Not applicable, this was not asked in Germany	0	158	0	0	0	158
...sudden flashes of light						
Yes*	43 (38) [29 - 47]	87 (55) [47 - 63]	106 (63) [55 - 70]	92 (54) [47 - 62]	85 (52) [44 - 60]	413 (53) [50 - 57]
No	54 (47)	41 (26)	45 (27)	40 (24)	55 (34)	235 (30)
I don't know	17 (15)	30 (19)	17 (10)	37 (22)	24 (15)	125 (16)
...sudden appearance or increase in moving spots (known as floaters)						
Yes*	62 (54) [45 - 64]	106 (67) [59 - 74]	129 (77) [70 - 83]	119 (70) [63 - 77]	113 (69) [61 - 76]	529 (68) [65 - 72]
No	35 (31)	38 (24)	25 (15)	24 (14)	42 (26)	164 (21)
I don't know	17 (15)	14 (9)	14 (8)	26 (15)	9 (5)	80 (10)
...cloudy or blurred vision						
Yes*	80 (70) [61 - 78]	123 (78) [71 - 84]	128 (76) [69 - 82]	117 (69) [62 - 76]	118 (72) [64 - 79]	566 (73) [70 - 76]
No	25 (22)	20 (13)	24 (14)	33 (20)	38 (23)	140 (18)

Table 3. Patient Knowledge: Possible Side Effects, Overall and by Country

Question	France (N = 114) n (%) [95% CI]	Germany (N = 158) n (%) [95% CI]	Italy (N = 168) n (%) [95% CI]	Spain (N = 169) n (%) [95% CI]	UK (N = 164) n (%) [95% CI]	Overall (N = 773) n (%) [95% CI]
I don't know	9 (8)	15 (9)	16 (10)	19 (11)	8 (5)	67 (9)
...sensitivity to light						
Yes*	72 (63) [54 - 72]	100 (63) [55 - 71]	129 (77) [70 - 83]	110 (65) [57 - 72]	107 (65) [57 - 72]	518 (67) [64 - 70]
No	34 (30)	39 (25)	20 (12)	31 (18)	46 (28)	170 (22)
I don't know	8 (7)	19 (12)	19 (11)	28 (17)	11 (7)	85 (11)
...an eye infection						
Yes*	55 (48) [39 - 58]	99 (63) [55 - 70]	123 (73) [66 - 80]	100 (59) [51 - 67]	96 (59) [51 - 66]	473 (61) [58 - 65]
No	47 (41)	38 (24)	31 (18)	39 (23)	55 (34)	210 (27)
I don't know	12 (11)	21 (13)	14 (8)	30 (18)	13 (8)	90 (12)
Number of correct responses selected among the ten Yes/No questions listed above						
0	0 (0)	2 (1)	3 (2)	5 (3)	1 (1)	11 (1)
1	3 (3)	14 (9)	3 (2)	8 (5)	14 (9)	42 (5)
2	8 (7)	6 (4)	6 (4)	5 (3)	6 (4)	31 (4)
3	15 (13)	15 (9)	10 (6)	15 (9)	10 (6)	65 (8)
4	15 (13)	16 (10)	11 (7)	13 (8)	14 (9)	69 (9)
5	18 (16)	20 (13)	12 (7)	20 (12)	12 (7)	82 (11)
6	21 (18)	15 (9)	19 (11)	15 (9)	21 (13)	91 (12)
7	10 (9)	24 (15)	15 (9)	19 (11)	27 (16)	95 (12)
8	11 (10)	34 (22)	22 (13)	19 (11)	25 (15)	111 (14)
9	8 (7)	12 (8)	57 (34)	41 (24)	30 (18)	148 (19)
10	5 (4)	0 (0)	10 (6)	9 (5)	4 (2)	28 (4)

Table 4. Patient Knowledge: Appropriate Action in Response to Side Effects, Overall and by Country

	France (N = 114)	Germany (N = 158)	Italy (N = 168)	Spain (N = 169)	UK (N = 164)	Overall (N = 773)
What should you do if you think you might be having a side effect from your Eylea injection? (Q3)	**n (%) [95% CI]**	**n (%) [95% CI]**	**n (%) [95% CI]**	**n (%) [95% CI]**	**n (%) [95% CI]**	**n (%) [95% CI]**
Speak to your ophthalmologist (or someone in his or her office) immediately*	78 (68) [59 - 77]	130 (82) [75 - 88]	154 (92) [86 - 95]	132 (78) [71 - 84]	110 (67) [59 - 74]	604 (78) [75 - 81]
Wait 48 hours to see if the symptoms improve	32 (28)	25 (16)	13 (8)	22 (13)	48 (29)	140 (18)
None of the above	2 (2)	0 (0)	1 (1)	11 (7)	3 (2)	17 (2)
I don't know	2 (2)	3 (2)	0 (0)	4 (2)	3 (2)	12 (2)

Table 5. Patient Pre-injection Instructions and Receipt of Aflibercept Educational Materials, Overall and by Country

Question	France (N = 114) n (%)	Germany (N = 158) n (%)	Italy (N = 168) n (%)	Spain (N = 169) n (%)	UK (N = 164) n (%)	Overall (N = 773) n (%)
Before your first injection of Eylea, did your ophthalmologist (or someone in his or her office) tell you what to expect during and after the injection? (Q4)						
Yes	77 (68)	102 (65)	135 (80)	111 (66)	120 (73)	545 (71)
No	22 (19)	43 (27)	18 (11)	39 (23)	26 (16)	148 (19)
I don't know or I don't remember	15 (13)	13 (8)	15 (9)	19 (11)	18 (11)	80 (10)
For the next question, I am going to show you some information materials. For each item, please tell me if you have been given it or not. (Q5)						
Patient Booklet, “Your Guide to EYLEA”						
Yes	4 (4)	81 (51)	103 (61)	31 (18)	72 (44)	291 (38)
No	93 (82)	67 (42)	55 (33)	134 (79)	80 (49)	429 (55)
I don't know or I don't remember	17 (15)	10 (6)	10 (6)	4 (2)	12 (7)	53 (7)
Audio CD						
Yes	1 (1)	32 (20)	67 (40)	23 (14)	54 (33)	177 (23)
No	108 (95)	109 (69)	86 (51)	145 (86)	99 (60)	547 (71)
I don't know or I don't remember	5 (4)	12 (8)	15 (9)	1 (1)	11 (7)	44 (6)
No answer	0 (0)	5 (3)	0 (0)	0 (0)	0 (0)	5 (1)
Patient Information Leaflet						
Yes	30 (26)	37 (23)	113 (67)	21 (12)	68 (41)	269 (35)
No	69 (61)	99 (63)	45 (27)	138 (82)	77 (47)	428 (55)
I don't know or I don't remember	15 (13)	19 (12)	10 (6)	9 (5)	19 (12)	72 (9)
No answer	0 (0)	3 (2)	0 (0)	1 (1)	0 (0)	4 (1)
Did your ophthalmologist (or someone in his or her office) give you any other information materials about Eylea that are not included here? (Q6a)						
Yes	22 (19)	8 (5)	13 (8)	12 (7)	26 (16)	81 (10)
No	78 (68)	131 (83)	136 (81)	138 (82)	118 (72)	601 (78)
I don't know or I don't remember	14 (12)	19 (12)	19 (11)	18 (11)	20 (12)	90 (12)
No answer	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	1 (0)

Table 6. Patient Use of Aflibercept Educational Materials, Overall and by Country

Question	France (N = 114) n (%)	Germany (N = 158) n (%)	Italy (N = 168) n (%)	Spain (N = 169) n (%)	UK (N = 164) n (%)	Overall (N = 773) n (%)
Did you read or listen to any of the Eylea materials? (Q7) [Interviewer note: Show the patient each piece of material that they have received based on response to Q5 and Q6B.]						
Patient Booklet, “Your Guide to EYLEA”						
Yes	4 (100)	65 (80)	98 (95)	18 (58)	64 (89)	249 (86)
No	0 (0)	10 (12)	4 (4)	12 (39)	6 (8)	32 (11)
I don't know or I don't remember	0 (0)	6 (7)	1 (1)	1 (3)	2 (3)	10 (3)
Not applicable skip pattern (did not indicate they received patient booklet)	110	77	65	138	92	482
Audio CD						
Yes	1 (100)	10 (31)	31 (46)	11 (48)	16 (30)	69 (39)
No	0 (0)	22 (69)	36 (54)	12 (52)	38 (70)	108 (61)
Not applicable skip pattern (did not indicate they received audio CD)	113	126	101	146	110	596
Patient Information Leaflet						
Yes	24 (80)	25 (68)	89 (79)	13 (62)	56 (82)	207 (77)
No	6 (20)	10 (27)	19 (17)	7 (33)	8 (12)	50 (19)
I don't know or I don't remember	0 (0)	2 (5)	5 (4)	1 (5)	4 (6)	12 (4)
Not applicable skip pattern (did not indicate they received patient information leaflet)	84	121	55	148	96	504
Other information materials (from Q6b)						
Yes	19 (86)	5 (63)	13 (100)	7 (58)	23 (88)	67 (83)
No	3 (14)	1 (13)	0 (0)	3 (25)	1 (4)	8 (10)
I don't know or I don't remember	0 (0)	0 (0)	0 (0)	1 (8)	1 (4)	2 (2)
No answer	0 (0)	2 (25)	0 (0)	1 (8)	1 (4)	4 (5)
Not applicable skip pattern (did not indicate they received any other materials)	92	150	155	157	138	692

Table 6. Patient Use of Aflibercept Educational Materials, Overall and by Country

Question	France (N = 114) n (%)	Germany (N = 158) n (%)	Italy (N = 168) n (%)	Spain (N = 169) n (%)	UK (N = 164) n (%)	Overall (N = 773) n (%)
Which of these Eylea information materials did you find the most useful? (Q8) [Interviewer note: Show the patient only the materials they have read from Q7.] (Please choose one answer only.)[a]						
Patient Booklet, Your Guide to EYLEA	3 (7)	50 (72)	68 (54)	10 (36)	48 (52)	179 (50)
Audio CD	1 (2)	5 (7)	13 (10)	8 (29)	5 (5)	32 (9)
Patient Information Leaflet	20 (48)	7 (10)	34 (27)	6 (21)	14 (15)	81 (23)
Item specified in Q6B	17 (40)	2 (3)	2 (2)	4 (14)	16 (17)	41 (11)
None	1 (2)	3 (4)	2 (2)	0 (0)	4 (4)	10 (3)
I don't know or I don't remember	1 (2)	4 (6)	9 (7)	0 (0)	8 (9)	22 (6)
No answer	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (0)
Not applicable skip pattern (in response to Q7 patient did not indicate they read any of the materials)	72	89	42	141	71	415
We would be interested in understanding any reasons that you did not read or listen to any of the Eylea information materials? (Q9) [Interviewer note: Let the patient respond and then select the response choices that fit. If needed, read response choices to the patient.] (Please choose all that apply.)						
You lost the materials	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	1 (2)
Someone else explained the information to you	3 (50)	3 (17)	1 (9)	2 (15)	1 (8)	10 (16)
You already knew the information	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	1 (2)
You don't typically read or listen to materials given to you by your doctor	0 (0)	1 (6)	2 (18)	2 (15)	3 (23)	8 (13)
You couldn't read them due to problems with your vision	0 (0)	2 (11)	3 (27)	4 (31)	2 (15)	11 (18)
The materials were too difficult to understand	0 (0)	4 (22)	0 (0)	0 (0)	0 (0)	4 (7)
The materials were too long	0 (0)	3 (17)	1 (9)	0 (0)	1 (8)	5 (8)

Table 6. Patient Use of Aflibercept Educational Materials, Overall and by Country

Question	France (N = 114) n (%)	Germany (N = 158) n (%)	Italy (N = 168) n (%)	Spain (N = 169) n (%)	UK (N = 164) n (%)	Overall (N = 773) n (%)
Other [specify]_____	0 (0)	6 (33)	1 (9)	4 (31)	3 (23)	14 (23)
I don't know or I don't remember	3 (50)	1 (6)	4 (36)	1 (8)	4 (31)	13 (21)
No answer	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	2 (0)
Not applicable skip pattern (in response to Q7 patient indicated they read or listened to at least one material)	42	69	126	28	93	358
Not applicable skip pattern (in response to Q5 and Q6 patient did not indicate they received any materials)	66	71	31	128	58	354

[a] Some patients selected more than one response to this question. Also, the results need to be interpreted with care as most people were not choosing between all 4 potential information sources because their choices were limited to the materials they indicated they read or viewed, per the previous question.

Listing of the two questions with open ended responses

If "Yes" to Q6a "Did your ophthalmologist (or someone in his or her office) give you any other information materials about Eylea that are not included here?" Response to Q6b "What else did they give you?"

Country	Patient Internal ID	Response
France	158	document pre injection
France	161	fiche explicative
France	352	protocole injections et reunions informations
France	352	SCHEMA THERAPEUTIQUE
France	352	reunions de patients
France	353	protocole injection
France	353	SCHEMA THERAPEUTIQUE
France	355	SCHEMAS THERAPEUTIQUE
France	357	SCHEMAS THERAPEUTIQUE
France	358	SCHEMA THERAPEUTIQUE
France	359	SCHEMA THERAPEUTIQUE
France	360	SCHEMAS THERAPEUTIQUE
France	362	SCHEMA THERAPEUTIQUE
France	366	SCHEMA THERAPEUTIQUE
France	422	fiche informative n°65 SFO
France	425	fiche d'information IVT
France	426	fiche information SFO n°65
France	427	fiche information SFO n°65
France	428	fiche information SFO n°65
France	430	fiche information SFO N°65
France	744	Fiches Gris Amsler
France	758	Non
France	763	non
France	764	Notice de la boite de traitement Eylea
France	849	fiche information sfo n°65
Germany	30	Tochter hat Infos aus Internet gegeben.
Germany	46	keine Angaben
Germany	54	Zusätzliche Aufklärung telefonisch
Germany	121	andere einzelne Produktinformation
Germany	232	weiß nicht mehr
Germany	241	Weiß nicht mehr. so lange her.
Germany	242	Material an der Anmeldung erhalten, Beschreibung d. mögl. 3 Medikamente, Infoblatt
Italy	213	spiegazione/opuscolo farmaco
Italy	433	opuscolo informato
Italy	435	foglio informativo - cons.informato
Italy	436	opuscolo informativo
Italy	438	opuscolo informativo
Italy	443	opuscolo informativo
Italy	444	opuscolo
Italy	445	opuscolo

Italy	537	consenso informato
Italy	573	Nota informativa
Italy	603	consenso informato medico-legale, istruzioni per laterapia post-operatoria
Italy	777	consenso informato dettagliato
Italy	778	consenso informato dettagliato
Spain	244	consentimiento informado
Spain	246	consentimiento informado
Spain	255	información del fármaco diferente a las mostradas
Spain	256	información del fármaco diferente a las mostradas
Spain	326	papeles adicionales , no sabe decirnos más
Spain	331	Hoja adicional en el consentimiento informado del pinchazo
Spain	479	unos folletos con explicacion de los efectos secundarios.
Spain	482	"Un folleto informativo dentro del cual estaba el material sobre Eylea"
Spain	485	Protocolo de inyecciones intravitreas
Spain	489	CONSENTIMIENTO
Spain	599	Consentimiento informado
Spain	836	consentimieto informado e información del fármaco
UK	146	verbal information
UK	147	verbal info
UK	169	Just verbally explained all about the procedure. Mr Kelly gave very good information.
UK	184	Pt. wanted me to put verbal information
UK	197	Leaflet
UK	260	Vebal advice on how the injection would work
UK	261	Verbal advice
UK	263	Consent form for Aflibercept 'Eylea' treatment with information of side effects that require reporting
UK	264	a pamphlet
UK	265	NHS consent form for Aflibercept treatment
UK	266	Patient consent for Aflibercept Eylea treatment
UK	268	Advice on self help groups for macular degeneration and information on macular degeneration
UK	270	Sheets with squares on to see if the lines were wavy
UK	276	Information on the injection process
UK	283	Information letters/paperwork.
UK	305	Verbal information
UK	306	Verbal information
UK	337	Unspecified Manchester Royal Eye Hospital Brochure
UK	340	Trust Brochure about Eye Treatment
UK	343	NHS Trust Eylea leaflet
UK	345	NHS Trust Leaflets (Eylea and Macular Degeneration)
UK	347	NHS Trust Eylea Leaflet
UK	349	NHS Trust Eylea Leaflet
UK	350	NHS Trust Eylea Leaflet
UK	415	a different version of eylea booklet
UK	505	talking from the consultant

If "Other" to Q9 "We would be interested in understanding any reasons that you did not read or listen to any of the Eylea information materials?"

Country	Patient Internal ID	Response
Germany	22	nicht ganz gelesen
Germany	109	Informationen waren teilweise schon bekannt
Germany	198	nicht erhalten
Germany	211	Pat. hatte Audio CD nicht
Germany	621	Kein Interesse
Germany	783	wollte Unsicherheiten vermeiden, vertraue meinem Arzt
Italy	215	per paura pereferisce non avere informazioni precise
Spain	294	No tenía reproductor de CD
Spain	331	no se proporciono
Spain	479	olvido
Spain	484	FALTA DE TIEMPO
UK	197	I wasn't given any
UK	315	not interested due to poor health
UK	494	rather not know and just have treatment

Annex 8. Analysis Tables for Patients (Other Stratification Variables)

Tables

Table 2a. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Received/Read Booklet

Question	Read (N = 249) n (%)	Received, Did Not Read or Does Not Remember (N = 42) n (%)	Did Not Receive (N = 429) n (%)	Doesn't Remember If Received (N = 53) n (%)
Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Q1)				
Any current eye problems (for example, infection, pain or redness in the eye)				
Yes*	236 (95)	38 (90)	389 (91)	47 (89)
No	12 (5)	4 (10)	31 (7)	3 (6)
I don't know	1 (0)	0 (0)	9 (2)	3 (6)
Any allergies to medications (for example, iodine or painkillers)				
Yes*	232 (93)	38 (90)	380 (89)	45 (85)
No	12 (5)	2 (5)	39 (9)	3 (6)
I don't know	5 (2)	2 (5)	10 (2)	5 (9)
Any problems with eye injections in the past				
Yes*	224 (90)	38 (90)	385 (90)	43 (81)
No	19 (8)	3 (7)	36 (8)	3 (6)
I don't know	6 (2)	1 (2)	8 (2)	6 (11)
No answer	0 (0)	0 (0)	0 (0)	1 (2)
If you have glaucoma or have had issues with feeling of high pressure in the eye in the past				
Yes*	223 (90)	39 (93)	361 (84)	43 (81)
No	17 (7)	1 (2)	39 (9)	5 (9)
I don't know	9 (4)	2 (5)	28 (7)	5 (9)
No answer	0 (0)	0 (0)	1 (0)	0 (0)

Table 2a. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Received/Read Booklet

Question	Read (N = 249) n (%)	Received, Did Not Read or Does Not Remember (N = 42) n (%)	Did Not Receive (N = 429) n (%)	Doesn't Remember If Received (N = 53) n (%)
If you see flashes of light				
Yes*	223 (90)	36 (86)	375 (87)	43 (81)
No	20 (8)	3 (7)	36 (8)	5 (9)
I don't know	6 (2)	2 (5)	18 (4)	5 (9)
No answer	0 (0)	1 (2)	0 (0)	0 (0)
If you see moving spots (known as floaters) in your eye				
Yes*	224 (90)	39 (93)	366 (85)	44 (83)
No	18 (7)	2 (5)	48 (11)	5 (9)
I don't know	7 (3)	0 (0)	15 (3)	4 (8)
No answer	0 (0)	1 (2)	0 (0)	0 (0)
Any medications that you have used				
Yes*	225 (90)	38 (90)	350 (82)	42 (79)
No	16 (6)	3 (7)	54 (13)	1 (2)
I don't know	8 (3)	1 (2)	25 (6)	10 (19)
If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection				
Yes*	227 (91)	38 (90)	374 (87)	43 (81)
No	18 (7)	4 (10)	41 (10)	4 (8)
I don't know	4 (2)	0 (0)	14 (3)	6 (11)
If you are pregnant, are planning to become pregnant, or are breastfeeding				
Yes*	148 (59)	24 (57)	203 (47)	24 (45)
No	56 (22)	14 (33)	132 (31)	18 (34)
I don't know	39 (16)	3 (7)	89 (21)	9 (17)
No answer	6 (2)	1 (2)	5 (1)	2 (4)

Table 2a. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Received/Read Booklet

Question	Read (N = 249) n (%)	Received, Did Not Read or Does Not Remember (N = 42) n (%)	Did Not Receive (N = 429) n (%)	Doesn't Remember If Received (N = 53) n (%)
Number of correct responses selected among the nine Yes/No questions listed above				
0	0 (0)	0 (0)	3 (1)	2 (4)
1	3 (1)	1 (2)	2 (0)	1 (2)
2	3 (1)	1 (2)	7 (2)	0 (0)
3	2 (1)	1 (2)	10 (2)	1 (2)
4	10 (4)	0 (0)	12 (3)	2 (4)
5	9 (4)	0 (0)	19 (4)	5 (9)
6	10 (4)	2 (5)	44 (10)	2 (4)
7	19 (8)	5 (12)	66 (15)	10 (19)
8	68 (27)	13 (31)	126 (29)	15 (28)
9	125 (50)	19 (45)	140 (33)	15 (28)

Table 3a. Patient Knowledge: Possible Side Effects, by Received/Read Booklet

Question	Read (N = 249) n (%)	Received, Did Not Read or Does Not Remember (N = 42) n (%)	Did Not Receive (N = 429) n (%)	Doesn't Remember If Received (N = 53) n (%)
We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] possible side effect of Eylea? (Q2)				
...a red or bloodshot eye				
Yes*	203 (82)	27 (64)	277 (65)	36 (68)
No	31 (12)	10 (24)	96 (22)	7 (13)
I don't know	15 (6)	5 (12)	56 (13)	10 (19)
...nausea and vomiting (feeling or being sick)				
Yes	99 (40)	13 (31)	105 (24)	11 (21)
No*	110 (44)	20 (48)	251 (59)	30 (57)
I don't know	40 (16)	9 (21)	73 (17)	12 (23)
...eye pain				
Yes*	206 (83)	29 (69)	297 (69)	37 (70)
No	38 (15)	11 (26)	102 (24)	9 (17)
I don't know	5 (2)	2 (5)	30 (7)	7 (13)
...detachment of the gel-like substance inside the eye from the retina				
Yes*	133 (53)	17 (40)	158 (37)	17 (32)
No	51 (20)	12 (29)	140 (33)	15 (28)
I don't know	65 (26)	13 (31)	131 (31)	21 (40)
...seeing halos around lights				
Yes*	129 (70)	16 (62)	179 (49)	25 (58)
No	34 (18)	7 (27)	120 (33)	9 (21)
I don't know	21 (11)	3 (12)	63 (17)	9 (21)
Not applicable, this was not asked in Germany	65	16	67	10

Table 3a. Patient Knowledge: Possible Side Effects, by Received/Read Booklet

Question	Read (N = 249) n (%)	Received, Did Not Read or Does Not Remember (N = 42) n (%)	Did Not Receive (N = 429) n (%)	Doesn't Remember If Received (N = 53) n (%)
...sudden flashes of light				
Yes*	166 (67)	25 (60)	198 (46)	24 (45)
No	52 (21)	11 (26)	158 (37)	14 (26)
I don't know	31 (12)	6 (14)	73 (17)	15 (28)
...sudden appearance or increase in moving spots (known as floaters)				
Yes*	201 (81)	28 (67)	266 (62)	34 (64)
No	34 (14)	7 (17)	112 (26)	11 (21)
I don't know	14 (6)	7 (17)	51 (12)	8 (15)
...cloudy or blurred vision				
Yes*	206 (83)	27 (64)	297 (69)	36 (68)
No	30 (12)	8 (19)	96 (22)	6 (11)
I don't know	13 (5)	7 (17)	36 (8)	11 (21)
...sensitivity to light				
Yes*	192 (77)	29 (69)	261 (61)	36 (68)
No	38 (15)	10 (24)	113 (26)	9 (17)
I don't know	19 (8)	3 (7)	55 (13)	8 (15)
...an eye infection				
Yes*	195 (78)	25 (60)	225 (52)	28 (53)
No	38 (15)	9 (21)	142 (33)	21 (40)
I don't know	16 (6)	8 (19)	62 (14)	4 (8)

Table 3a. Patient Knowledge: Possible Side Effects, by Received/Read Booklet

Question	Read (N = 249) n (%)	Received, Did Not Read or Does Not Remember (N = 42) n (%)	Did Not Receive (N = 429) n (%)	Doesn't Remember If Received (N = 53) n (%)
Number of correct responses selected among the ten Yes/No questions listed above				
0	1 (0)	2 (5)	5 (1)	3 (6)
1	7 (3)	2 (5)	32 (7)	1 (2)
2	5 (2)	1 (2)	25 (6)	0 (0)
3	12 (5)	4 (10)	46 (11)	3 (6)
4	18 (7)	3 (7)	40 (9)	8 (15)
5	18 (7)	7 (17)	48 (11)	9 (17)
6	23 (9)	4 (10)	53 (12)	11 (21)
7	32 (13)	5 (12)	53 (12)	5 (9)
8	45 (18)	7 (17)	55 (13)	4 (8)
9	76 (31)	5 (12)	60 (14)	7 (13)
10	12 (5)	2 (5)	12 (3)	2 (4)

Table 4a. Patient Knowledge: Appropriate Action in Response to Side Effects, by Received/Read Booklet

	Read (N = 249)	Received, Did Not Read or Does Not Remember (N = 42)	Did Not Receive (N = 429)	Doesn't Remember If Received (N = 53)
What should you do if you think you might be having a side effect from your Eylea injection? (Q3)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Speak to your ophthalmologist (or someone in his or her office) immediately*	217 (87)	33 (79)	318 (74)	36 (68)
Wait 48 hours to see if the symptoms improve	30 (12)	9 (21)	88 (21)	13 (25)
None of the above	1 (0)	0 (0)	16 (4)	0 (0)
I don't know	1 (0)	0 (0)	7 (2)	4 (8)

Tables

Table 2b. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_1N

Question	How often do you need to have someone other than your doctor or nurse READ information materials to you				
	None of the time (N = 514) n (%)	Some of the time (N = 120) n (%)	Most of the time (N = 51) n (%)	All of the time (N = 74) n (%)	I don't know (N = 14) n (%)
Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Q1)					
Any current eye problems (for example, infection, pain or redness in the eye)					
Yes*	472 (92)	112 (93)	48 (94)	66 (89)	12 (86)
No	34 (7)	8 (7)	3 (6)	3 (4)	2 (14)
I don't know	8 (2)	0 (0)	0 (0)	5 (7)	0 (0)
Any allergies to medications (for example, iodine or painkillers)					
Yes*	466 (91)	105 (88)	46 (90)	66 (89)	12 (86)
No	37 (7)	9 (8)	3 (6)	5 (7)	2 (14)
I don't know	11 (2)	6 (5)	2 (4)	3 (4)	0 (0)
Any problems with eye injections in the past					
Yes*	475 (92)	106 (88)	43 (84)	56 (76)	10 (71)
No	30 (6)	13 (11)	3 (6)	11 (15)	4 (29)
I don't know	8 (2)	1 (1)	5 (10)	7 (9)	0 (0)
No answer	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)
If you have glaucoma or have had issues with feeling of high pressure in the eye in the past					
Yes*	458 (89)	98 (82)	41 (80)	57 (77)	12 (86)
No	36 (7)	11 (9)	4 (8)	9 (12)	2 (14)
I don't know	19 (4)	11 (9)	6 (12)	8 (11)	0 (0)
No answer	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table 2b. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_1N

Question	How often do you need to have someone other than your doctor or nurse READ information materials to you				
	None of the time (N = 514) n (%)	Some of the time (N = 120) n (%)	Most of the time (N = 51) n (%)	All of the time (N = 74) n (%)	I don't know (N = 14) n (%)
If you see flashes of light					
Yes*	467 (91)	98 (82)	40 (78)	61 (82)	11 (79)
No	34 (7)	15 (13)	6 (12)	7 (9)	2 (14)
I don't know	13 (3)	6 (5)	5 (10)	6 (8)	1 (7)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
If you see moving spots (known as floaters) in your eye					
Yes*	456 (89)	102 (85)	45 (88)	59 (80)	11 (79)
No	46 (9)	8 (7)	6 (12)	10 (14)	3 (21)
I don't know	12 (2)	9 (8)	0 (0)	5 (7)	0 (0)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Any medications that you have used					
Yes*	448 (87)	94 (78)	37 (73)	65 (88)	11 (79)
No	47 (9)	14 (12)	8 (16)	3 (4)	2 (14)
I don't know	19 (4)	12 (10)	6 (12)	6 (8)	1 (7)
If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection					
Yes*	465 (90)	101 (84)	44 (86)	61 (82)	11 (79)
No	39 (8)	14 (12)	3 (6)	9 (12)	2 (14)
I don't know	10 (2)	5 (4)	4 (8)	4 (5)	1 (7)
If you are pregnant, are planning to become pregnant, or are breastfeeding					
Yes*	273 (53)	56 (47)	27 (53)	35 (47)	8 (57)
No	150 (29)	37 (31)	12 (24)	18 (24)	3 (21)
I don't know	81 (16)	23 (19)	12 (24)	21 (28)	3 (21)
No answer	10 (2)	4 (3)	0 (0)	0 (0)	0 (0)

Table 2b. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_1N

	How often do you need to have someone other than your doctor or nurse READ information materials to you				
Question	**None of the time (N = 514) n (%)**	**Some of the time (N = 120) n (%)**	**Most of the time (N = 51) n (%)**	**All of the time (N = 74) n (%)**	**I don't know (N = 14) n (%)**
Number of correct responses selected among the nine Yes/No questions listed above					
0	2 (0)	0 (0)	0 (0)	3 (4)	0 (0)
1	3 (1)	2 (2)	1 (2)	0 (0)	1 (7)
2	7 (1)	2 (2)	0 (0)	1 (1)	1 (7)
3	7 (1)	2 (2)	2 (4)	3 (4)	0 (0)
4	13 (3)	4 (3)	2 (4)	3 (4)	2 (14)
5	16 (3)	9 (8)	5 (10)	3 (4)	0 (0)
6	32 (6)	14 (12)	3 (6)	9 (12)	0 (0)
7	67 (13)	19 (16)	7 (14)	7 (9)	0 (0)
8	154 (30)	30 (25)	15 (29)	20 (27)	3 (21)
9	213 (41)	38 (32)	16 (31)	25 (34)	7 (50)

Table 3b. Patient Knowledge: Possible Side Effects, by by Q12_1N

Question	How often do you need to have someone other than your doctor or nurse READ information materials to you				
	None of the time (N = 514) n (%)	Some of the time (N = 120) n (%)	Most of the time (N = 51) n (%)	All of the time (N = 74) n (%)	I don't know (N = 14) n (%)
We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] possible side effect of Eylea? (Q2)					
...a red or bloodshot eye					
Yes*	373 (73)	79 (66)	40 (78)	46 (62)	5 (36)
No	89 (17)	23 (19)	8 (16)	16 (22)	8 (57)
I don't know	52 (10)	18 (15)	3 (6)	12 (16)	1 (7)
...nausea and vomiting (feeling or being sick)					
Yes	160 (31)	34 (28)	16 (31)	14 (19)	4 (29)
No*	277 (54)	62 (52)	21 (41)	42 (57)	9 (64)
I don't know	77 (15)	24 (20)	14 (27)	18 (24)	1 (7)
...eye pain					
Yes*	388 (75)	80 (67)	42 (82)	51 (69)	8 (57)
No	104 (20)	30 (25)	7 (14)	14 (19)	5 (36)
I don't know	22 (4)	10 (8)	2 (4)	9 (12)	1 (7)
...detachment of the gel-like substance inside the eye from the retina					
Yes*	224 (44)	45 (38)	24 (47)	28 (38)	4 (29)
No	140 (27)	39 (33)	13 (25)	20 (27)	6 (43)
I don't know	150 (29)	36 (30)	14 (27)	26 (35)	4 (29)
...seeing halos around lights					
Yes*	231 (58)	57 (59)	24 (52)	35 (53)	2 (25)
No	113 (28)	25 (26)	8 (17)	20 (30)	4 (50)
I don't know	54 (14)	15 (15)	14 (30)	11 (17)	2 (25)
Not applicable, this was not asked in Germany	116	23	5	8	6

Table 3b. Patient Knowledge: Possible Side Effects, by by Q12_1N

	How often do you need to have someone other than your doctor or nurse READ information materials to you				
Question	**None of the time (N = 514) n (%)**	**Some of the time (N = 120) n (%)**	**Most of the time (N = 51) n (%)**	**All of the time (N = 74) n (%)**	**I don't know (N = 14) n (%)**
...sudden flashes of light					
Yes*	275 (54)	66 (55)	29 (57)	36 (49)	7 (50)
No	160 (31)	38 (32)	10 (20)	22 (30)	5 (36)
I don't know	79 (15)	16 (13)	12 (24)	16 (22)	2 (14)
...sudden appearance or increase in moving spots (known as floaters)					
Yes*	359 (70)	82 (68)	36 (71)	46 (62)	6 (43)
No	110 (21)	22 (18)	7 (14)	17 (23)	8 (57)
I don't know	45 (9)	16 (13)	8 (16)	11 (15)	0 (0)
...cloudy or blurred vision					
Yes*	386 (75)	89 (74)	37 (73)	47 (64)	7 (50)
No	96 (19)	16 (13)	7 (14)	16 (22)	5 (36)
I don't know	32 (6)	15 (13)	7 (14)	11 (15)	2 (14)
...sensitivity to light					
Yes*	358 (70)	71 (59)	35 (69)	46 (62)	8 (57)
No	109 (21)	29 (24)	9 (18)	18 (24)	5 (36)
I don't know	47 (9)	20 (17)	7 (14)	10 (14)	1 (7)
...an eye infection					
Yes*	332 (65)	68 (57)	32 (63)	37 (50)	4 (29)
No	135 (26)	33 (28)	13 (25)	22 (30)	7 (50)
I don't know	47 (9)	19 (16)	6 (12)	15 (20)	3 (21)

Table 3b. Patient Knowledge: Possible Side Effects, by by Q12_1N

	How often do you need to have someone other than your doctor or nurse READ information materials to you				
Question	**None of the time (N = 514) n (%)**	**Some of the time (N = 120) n (%)**	**Most of the time (N = 51) n (%)**	**All of the time (N = 74) n (%)**	**I don't know (N = 14) n (%)**
Number of correct responses selected among the ten Yes/No questions listed above					
0	3 (1)	2 (2)	0 (0)	6 (8)	0 (0)
1	29 (6)	6 (5)	2 (4)	3 (4)	2 (14)
2	19 (4)	5 (4)	1 (2)	5 (7)	1 (7)
3	41 (8)	11 (9)	5 (10)	5 (7)	3 (21)
4	45 (9)	11 (9)	4 (8)	6 (8)	3 (21)
5	49 (10)	16 (13)	6 (12)	10 (14)	1 (7)
6	59 (11)	14 (12)	10 (20)	8 (11)	0 (0)
7	64 (12)	19 (16)	4 (8)	5 (7)	3 (21)
8	81 (16)	16 (13)	5 (10)	9 (12)	0 (0)
9	102 (20)	19 (16)	13 (25)	13 (18)	1 (7)
10	22 (4)	1 (1)	1 (2)	4 (5)	0 (0)

Table 4b. Patient Knowledge: Appropriate Action in Response to Side Effects, by by Q12_1N

	How often do you need to have someone other than your doctor or nurse READ information materials to you				
What should you do if you think you might be having a side effect from your Eylea injection? (Q3)	**None of the time (N = 514) n (%)**	**Some of the time (N = 120) n (%)**	**Most of the time (N = 51) n (%)**	**All of the time (N = 74) n (%)**	**I don't know (N = 14) n (%)**
Speak to your ophthalmologist (or someone in his or her office) immediately*	409 (80)	93 (78)	41 (80)	50 (68)	11 (79)
Wait 48 hours to see if the symptoms improve	88 (17)	21 (18)	9 (18)	20 (27)	2 (14)
None of the above	12 (2)	2 (2)	1 (2)	2 (3)	0 (0)
I don't know	5 (1)	4 (3)	0 (0)	2 (3)	1 (7)

Tables

Table 2c. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_2N

	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
Question	**None of the time (N = 512) n (%)**	**Some of the time (N = 150) n (%)**	**Most of the time (N = 41) n (%)**	**All of the time (N = 58) n (%)**	**I don't know (N = 12) n (%)**
Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Q1)					
Any current eye problems (for example, infection, pain or redness in the eye)					
Yes*	470 (92)	140 (93)	37 (90)	53 (91)	10 (83)
No	33 (6)	9 (6)	4 (10)	2 (3)	2 (17)
I don't know	9 (2)	1 (1)	0 (0)	3 (5)	0 (0)
Any allergies to medications (for example, iodine or painkillers)					
Yes*	464 (91)	134 (89)	38 (93)	49 (84)	10 (83)
No	39 (8)	10 (7)	2 (5)	4 (7)	1 (8)
I don't know	9 (2)	6 (4)	1 (2)	5 (9)	1 (8)
Any problems with eye injections in the past					
Yes*	473 (92)	129 (86)	33 (80)	46 (79)	9 (75)
No	31 (6)	15 (10)	5 (12)	7 (12)	3 (25)
I don't know	7 (1)	6 (4)	3 (7)	5 (9)	0 (0)
No answer	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)
If you have glaucoma or have had issues with feeling of high pressure in the eye in the past					
Yes*	459 (90)	123 (82)	32 (78)	42 (72)	10 (83)
No	35 (7)	14 (9)	3 (7)	9 (16)	1 (8)
I don't know	17 (3)	13 (9)	6 (15)	7 (12)	1 (8)
No answer	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table 2c. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_2N

Question	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
	None of the time (N = 512) n (%)	Some of the time (N = 150) n (%)	Most of the time (N = 41) n (%)	All of the time (N = 58) n (%)	I don't know (N = 12) n (%)
If you see flashes of light					
Yes*	457 (89)	130 (87)	32 (78)	48 (83)	10 (83)
No	39 (8)	11 (7)	8 (20)	5 (9)	1 (8)
I don't know	16 (3)	8 (5)	1 (2)	5 (9)	1 (8)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
If you see moving spots (known as floaters) in your eye					
Yes*	459 (90)	122 (81)	37 (90)	46 (79)	9 (75)
No	39 (8)	20 (13)	4 (10)	8 (14)	2 (17)
I don't know	14 (3)	7 (5)	0 (0)	4 (7)	1 (8)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Any medications that you have used					
Yes*	441 (86)	120 (80)	33 (80)	51 (88)	10 (83)
No	50 (10)	19 (13)	2 (5)	2 (3)	1 (8)
I don't know	21 (4)	11 (7)	6 (15)	5 (9)	1 (8)
If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection					
Yes*	462 (90)	130 (87)	33 (80)	46 (79)	11 (92)
No	43 (8)	14 (9)	3 (7)	7 (12)	0 (0)
I don't know	7 (1)	6 (4)	5 (12)	5 (9)	1 (8)
If you are pregnant, are planning to become pregnant, or are breastfeeding					
Yes*	266 (52)	76 (51)	20 (49)	28 (48)	9 (75)
No	160 (31)	36 (24)	11 (27)	12 (21)	1 (8)
I don't know	75 (15)	35 (23)	10 (24)	18 (31)	2 (17)
No answer	11 (2)	3 (2)	0 (0)	0 (0)	0 (0)

Table 2c. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_2N

	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
Question	**None of the time (N = 512) n (%)**	**Some of the time (N = 150) n (%)**	**Most of the time (N = 41) n (%)**	**All of the time (N = 58) n (%)**	**I don't know (N = 12) n (%)**
Number of correct responses selected among the nine Yes/No questions listed above					
0	1 (0)	2 (1)	0 (0)	2 (3)	0 (0)
1	3 (1)	2 (1)	1 (2)	0 (0)	1 (8)
2	9 (2)	0 (0)	1 (2)	1 (2)	0 (0)
3	9 (2)	1 (1)	1 (2)	3 (5)	0 (0)
4	12 (2)	7 (5)	2 (5)	2 (3)	1 (8)
5	14 (3)	11 (7)	3 (7)	4 (7)	1 (8)
6	36 (7)	13 (9)	2 (5)	7 (12)	0 (0)
7	64 (13)	24 (16)	7 (17)	5 (9)	0 (0)
8	155 (30)	40 (27)	11 (27)	13 (22)	3 (25)
9	209 (41)	50 (33)	13 (32)	21 (36)	6 (50)

Table 3c. Patient Knowledge: Possible Side Effects, by by Q12_2N

Question	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
	None of the time (N = 512) n (%)	Some of the time (N = 150) n (%)	Most of the time (N = 41) n (%)	All of the time (N = 58) n (%)	I don't know (N = 12) n (%)
We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] possible side effect of Eylea? (Q2)					
...a red or bloodshot eye					
Yes*	370 (72)	106 (71)	24 (59)	36 (62)	7 (58)
No	92 (18)	26 (17)	11 (27)	11 (19)	4 (33)
I don't know	50 (10)	18 (12)	6 (15)	11 (19)	1 (8)
...nausea and vomiting (feeling or being sick)					
Yes	157 (31)	42 (28)	12 (29)	13 (22)	4 (33)
No*	275 (54)	78 (52)	20 (49)	32 (55)	6 (50)
I don't know	80 (16)	30 (20)	9 (22)	13 (22)	2 (17)
...eye pain					
Yes*	381 (74)	109 (73)	32 (78)	40 (69)	7 (58)
No	106 (21)	32 (21)	6 (15)	12 (21)	4 (33)
I don't know	25 (5)	9 (6)	3 (7)	6 (10)	1 (8)
...detachment of the gel-like substance inside the eye from the retina					
Yes*	223 (44)	57 (38)	13 (32)	27 (47)	5 (42)
No	146 (29)	42 (28)	13 (32)	13 (22)	4 (33)
I don't know	143 (28)	51 (34)	15 (37)	18 (31)	3 (25)
...seeing halos around lights					
Yes*	230 (57)	66 (57)	20 (53)	31 (60)	2 (33)
No	116 (29)	30 (26)	8 (21)	13 (25)	3 (50)
I don't know	57 (14)	20 (17)	10 (26)	8 (15)	1 (17)
Not applicable, this was not asked in Germany	109	34	3	6	6

Table 3c. Patient Knowledge: Possible Side Effects, by by Q12_2N

Question	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
	None of the time (N = 512) n (%)	Some of the time (N = 150) n (%)	Most of the time (N = 41) n (%)	All of the time (N = 58) n (%)	I don't know (N = 12) n (%)
...sudden flashes of light					
Yes*	270 (53)	85 (57)	22 (54)	30 (52)	6 (50)
No	164 (32)	45 (30)	7 (17)	16 (28)	3 (25)
I don't know	78 (15)	20 (13)	12 (29)	12 (21)	3 (25)
...sudden appearance or increase in moving spots (known as floaters)					
Yes*	352 (69)	106 (71)	26 (63)	40 (69)	5 (42)
No	112 (22)	28 (19)	7 (17)	10 (17)	7 (58)
I don't know	48 (9)	16 (11)	8 (20)	8 (14)	0 (0)
...cloudy or blurred vision					
Yes*	381 (74)	116 (77)	23 (56)	40 (69)	6 (50)
No	92 (18)	22 (15)	12 (29)	9 (16)	5 (42)
I don't know	39 (8)	12 (8)	6 (15)	9 (16)	1 (8)
...sensitivity to light					
Yes*	358 (70)	99 (66)	20 (49)	35 (60)	6 (50)
No	107 (21)	31 (21)	13 (32)	14 (24)	5 (42)
I don't know	47 (9)	20 (13)	8 (20)	9 (16)	1 (8)
...an eye infection					
Yes*	330 (64)	88 (59)	21 (51)	29 (50)	5 (42)
No	135 (26)	38 (25)	13 (32)	17 (29)	7 (58)
I don't know	47 (9)	24 (16)	7 (17)	12 (21)	0 (0)

Table 3c. Patient Knowledge: Possible Side Effects, by by Q12_2N

	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
Question	**None of the time (N = 512) n (%)**	**Some of the time (N = 150) n (%)**	**Most of the time (N = 41) n (%)**	**All of the time (N = 58) n (%)**	**I don't know (N = 12) n (%)**
Number of correct responses selected among the ten Yes/No questions listed above					
0	4 (1)	1 (1)	1 (2)	5 (9)	0 (0)
1	27 (5)	9 (6)	3 (7)	1 (2)	2 (17)
2	20 (4)	4 (3)	3 (7)	3 (5)	1 (8)
3	43 (8)	9 (6)	6 (15)	5 (9)	2 (17)
4	49 (10)	12 (8)	4 (10)	2 (3)	2 (17)
5	48 (9)	24 (16)	3 (7)	6 (10)	1 (8)
6	52 (10)	24 (16)	6 (15)	9 (16)	0 (0)
7	63 (12)	21 (14)	4 (10)	5 (9)	2 (17)
8	89 (17)	12 (8)	2 (5)	8 (14)	0 (0)
9	97 (19)	29 (19)	7 (17)	13 (22)	2 (17)
10	20 (4)	5 (3)	2 (5)	1 (2)	0 (0)

Table 4c. Patient Knowledge: Appropriate Action in Response to Side Effects, by by Q12_2N

	How often do you need to have someone other than your doctor or nurse EXPLAIN information materials to you				
What should you do if you think you might be having a side effect from your Eylea injection? (Q3)	**None of the time (N = 512) n (%)**	**Some of the time (N = 150) n (%)**	**Most of the time (N = 41) n (%)**	**All of the time (N = 58) n (%)**	**I don't know (N = 12) n (%)**
Speak to your ophthalmologist (or someone in his or her office) immediately*	405 (79)	119 (79)	31 (76)	39 (67)	10 (83)
Wait 48 hours to see if the symptoms improve	93 (18)	23 (15)	8 (20)	15 (26)	1 (8)
None of the above	9 (2)	5 (3)	1 (2)	2 (3)	0 (0)
I don't know	5 (1)	3 (2)	1 (2)	2 (3)	1 (8)

Tables

Table 2d. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
Question	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Q1)					
Any current eye problems (for example, infection, pain or redness in the eye)					
Yes*	562 (92)	86 (91)	26 (90)	27 (84)	9 (90)
No	38 (6)	6 (6)	2 (7)	3 (9)	1 (10)
I don't know	8 (1)	2 (2)	1 (3)	2 (6)	0 (0)
Any allergies to medications (for example, iodine or painkillers)					
Yes*	554 (91)	80 (85)	24 (83)	29 (91)	8 (80)
No	43 (7)	10 (11)	2 (7)	0 (0)	1 (10)
I don't know	11 (2)	4 (4)	3 (10)	3 (9)	1 (10)
Any problems with eye injections in the past					
Yes*	551 (91)	83 (88)	23 (79)	26 (81)	7 (70)
No	44 (7)	8 (9)	2 (7)	4 (13)	3 (30)
I don't know	12 (2)	3 (3)	4 (14)	2 (6)	0 (0)
No answer	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)
If you have glaucoma or have had issues with feeling of high pressure in the eye in the past					
Yes*	535 (88)	75 (80)	23 (79)	24 (75)	9 (90)
No	47 (8)	8 (9)	1 (3)	5 (16)	1 (10)
I don't know	25 (4)	11 (12)	5 (17)	3 (9)	0 (0)
No answer	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Table 2d. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
Question	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
If you see flashes of light					
Yes*	541 (89)	81 (86)	22 (76)	24 (75)	9 (90)
No	43 (7)	9 (10)	7 (24)	4 (13)	1 (10)
I don't know	24 (4)	3 (3)	0 (0)	4 (13)	0 (0)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
If you see moving spots (known as floaters) in your eye					
Yes*	537 (88)	79 (84)	23 (79)	25 (78)	9 (90)
No	53 (9)	10 (11)	6 (21)	3 (9)	1 (10)
I don't know	18 (3)	4 (4)	0 (0)	4 (13)	0 (0)
No answer	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Any medications that you have used					
Yes*	519 (85)	74 (79)	25 (86)	28 (88)	9 (90)
No	57 (9)	14 (15)	1 (3)	1 (3)	1 (10)
I don't know	32 (5)	6 (6)	3 (10)	3 (9)	0 (0)
If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection					
Yes*	545 (90)	78 (83)	25 (86)	24 (75)	10 (100)
No	53 (9)	9 (10)	1 (3)	4 (13)	0 (0)
I don't know	10 (2)	7 (7)	3 (10)	4 (13)	0 (0)
If you are pregnant, are planning to become pregnant, or are breastfeeding					
Yes*	313 (51)	47 (50)	15 (52)	16 (50)	8 (80)
No	180 (30)	23 (24)	7 (24)	9 (28)	1 (10)
I don't know	103 (17)	22 (23)	7 (24)	7 (22)	1 (10)
No answer	12 (2)	2 (2)	0 (0)	0 (0)	0 (0)

Table 2d. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
Question	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
Number of correct responses selected among the nine Yes/No questions listed above					
0	1 (0)	2 (2)	0 (0)	2 (6)	0 (0)
1	4 (1)	2 (2)	0 (0)	0 (0)	1 (10)
2	10 (2)	0 (0)	0 (0)	1 (3)	0 (0)
3	10 (2)	1 (1)	2 (7)	1 (3)	0 (0)
4	15 (2)	4 (4)	3 (10)	2 (6)	0 (0)
5	19 (3)	10 (11)	3 (10)	1 (3)	0 (0)
6	48 (8)	8 (9)	0 (0)	2 (6)	0 (0)
7	84 (14)	9 (10)	4 (14)	2 (6)	1 (10)
8	181 (30)	21 (22)	8 (28)	10 (31)	2 (20)
9	236 (39)	37 (39)	9 (31)	11 (34)	6 (60)

Table 3d. Patient Knowledge: Possible Side Effects, by by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
Question	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] possible side effect of Eylea? (Q2)					
...a red or bloodshot eye					
Yes*	432 (71)	65 (69)	19 (66)	22 (69)	5 (50)
No	108 (18)	20 (21)	7 (24)	5 (16)	4 (40)
I don't know	68 (11)	9 (10)	3 (10)	5 (16)	1 (10)
...nausea and vomiting (feeling or being sick)					
Yes	178 (29)	25 (27)	9 (31)	11 (34)	5 (50)
No*	334 (55)	42 (45)	15 (52)	15 (47)	5 (50)
I don't know	96 (16)	27 (29)	5 (17)	6 (19)	0 (0)
...eye pain					
Yes*	450 (74)	67 (71)	22 (76)	24 (75)	6 (60)
No	126 (21)	18 (19)	6 (21)	6 (19)	4 (40)
I don't know	32 (5)	9 (10)	1 (3)	2 (6)	0 (0)
...detachment of the gel-like substance inside the eye from the retina					
Yes*	262 (43)	32 (34)	12 (41)	14 (44)	5 (50)
No	170 (28)	29 (31)	8 (28)	7 (22)	4 (40)
I don't know	176 (29)	33 (35)	9 (31)	11 (34)	1 (10)
...seeing halos around lights					
Yes*	282 (59)	39 (51)	12 (46)	15 (54)	1 (25)
No	136 (28)	19 (25)	7 (27)	5 (18)	3 (75)
I don't know	63 (13)	18 (24)	7 (27)	8 (29)	0 (0)
Not applicable, this was not asked in Germany	127	18	3	4	6

Table 3d. Patient Knowledge: Possible Side Effects, by by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
Question	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
...sudden flashes of light					
Yes*	320 (53)	53 (56)	15 (52)	20 (63)	5 (50)
No	193 (32)	24 (26)	8 (28)	7 (22)	3 (30)
I don't know	95 (16)	17 (18)	6 (21)	5 (16)	2 (20)
...sudden appearance or increase in moving spots (known as floaters)					
Yes*	424 (70)	64 (68)	17 (59)	20 (63)	4 (40)
No	129 (21)	15 (16)	9 (31)	5 (16)	6 (60)
I don't know	55 (9)	15 (16)	3 (10)	7 (22)	0 (0)
...cloudy or blurred vision					
Yes*	451 (74)	72 (77)	17 (59)	21 (66)	5 (50)
No	110 (18)	14 (15)	8 (28)	4 (13)	4 (40)
I don't know	47 (8)	8 (9)	4 (14)	7 (22)	1 (10)
...sensitivity to light					
Yes*	426 (70)	56 (60)	10 (34)	20 (63)	6 (60)
No	126 (21)	20 (21)	14 (48)	7 (22)	3 (30)
I don't know	56 (9)	18 (19)	5 (17)	5 (16)	1 (10)
...an eye infection					
Yes*	376 (62)	59 (63)	17 (59)	18 (56)	3 (30)
No	169 (28)	19 (20)	8 (28)	8 (25)	6 (60)
I don't know	63 (10)	16 (17)	4 (14)	6 (19)	1 (10)

Table 3d. Patient Knowledge: Possible Side Effects, by by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
Question	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
Number of correct responses selected among the ten Yes/No questions listed above					
0	7 (1)	1 (1)	1 (3)	2 (6)	0 (0)
1	34 (6)	2 (2)	2 (7)	2 (6)	2 (20)
2	25 (4)	3 (3)	2 (7)	1 (3)	0 (0)
3	49 (8)	10 (11)	2 (7)	2 (6)	2 (20)
4	57 (9)	8 (9)	1 (3)	1 (3)	2 (20)
5	56 (9)	16 (17)	5 (17)	5 (16)	0 (0)
6	62 (10)	17 (18)	9 (31)	2 (6)	1 (10)
7	71 (12)	15 (16)	1 (3)	6 (19)	2 (20)
8	101 (17)	6 (6)	0 (0)	4 (13)	0 (0)
9	119 (20)	16 (17)	6 (21)	6 (19)	1 (10)
10	27 (4)	0 (0)	0 (0)	1 (3)	0 (0)

Table 4d. Patient Knowledge: Appropriate Action in Response to Side Effects, by by Q12_3N

	How often do you need to have someone other than your doctor or nurse MAKE TREATMENT DECISIONS for you				
What should you do if you think you might be having a side effect from your Eylea injection? (Q3)	**None of the time (N = 608) n (%)**	**Some of the time (N = 94) n (%)**	**Most of the time (N = 29) n (%)**	**All of the time (N = 32) n (%)**	**I don't know (N = 10) n (%)**
Speak to your ophthalmologist (or someone in his or her office) immediately*	479 (79)	76 (81)	20 (69)	22 (69)	7 (70)
Wait 48 hours to see if the symptoms improve	112 (18)	13 (14)	7 (24)	7 (22)	1 (10)
None of the above	12 (2)	2 (2)	2 (7)	1 (3)	0 (0)
I don't know	5 (1)	3 (3)	0 (0)	2 (6)	2 (20)

Annex 9. Analysis Tables for Recruiting Physicians (Overall and by Country)

Tables

Table 1. Physician Experience With Aflibercept, Overall and by Country

Question	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
Have you prescribed Eylea and/or administered an Eylea injection any patient in the past 6 months? (S1) Tick all that apply.						
Prescribed Eylea	6 (100)	10 (100)	10 (100)	8 (89)	11 (100)	45 (98)
Administered an Eylea injection	6 (100)	9 (90)	9 (90)	7 (78)	11 (100)	42 (91)
For which of the following indications have you prescribed and/or administered Eylea in the past 6 months? (S2) Tick all that apply.						
Neovascular (wet) age-related macular degeneration (wAMD)	6 (100)	10 (100)	10 (100)	9 (100)	11 (100)	46 (100)
Visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO)	5 (83)	9 (90)	6 (60)	8 (89)	10 (91)	38 (83)
Visual impairment due to diabetic macular oedema (DME)	5 (83)	9 (90)	8 (80)	9 (100)	10 (91)	41 (89)
Visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO)	6 (100)	9 (90)	2 (20)	8 (89)	2 (18)	27 (59)
Other indication	1 (17)	1 (10)	0 (0)	4 (44)	0 (0)	6 (13)
At your site, who has the primary responsibility for the preparation of an Eylea injection (i.e., opens the vial or pre-filled syringe[a] and prepares the syringe for injection)? (S4) Tick one answer.						
I am responsible	5 (83)	6 (60)	4 (40)	4 (44)	7 (64)	26 (57)
A specialized nurse	1 (17)	3 (30)	4 (40)	1 (11)	4 (36)	13 (28)
Pharmacy	0 (0)	1 (10)	1 (10)	4 (44)	0 (0)	6 (13)
Other	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	1 (2)
In the past 3 months, to how many patients have you prescribed and/or administered Eylea for the following indications? (Q25)						
wAMD						
1 to 5 patients	0 (0)	0 (0)	1 (10)	1 (11)	1 (9)	3 (7)
6 to 10 patients	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	1 (2)

Table 1. Physician Experience With Aflibercept, Overall and by Country

Question	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
11 to 20 patients	1 (17)	0 (0)	2 (20)	2 (22)	2 (18)	7 (15)
More than 20 patients	5 (83)	10 (100)	6 (60)	6 (67)	8 (73)	35 (76)
CRVO						
None	0 (0)	0 (0)	4 (40)	0 (0)	1 (9)	5 (11)
1 to 5 patients	4 (67)	0 (0)	6 (60)	3 (33)	5 (45)	18 (39)
6 to 10 patients	2 (33)	2 (20)	0 (0)	4 (44)	2 (18)	10 (22)
11 to 20 patients	0 (0)	3 (30)	0 (0)	2 (22)	1 (9)	6 (13)
More than 20 patients	0 (0)	5 (50)	0 (0)	0 (0)	2 (18)	7 (15)
BRVO						
None	0 (0)	0 (0)	6 (60)	0 (0)	9 (82)	15 (33)
1 to 5 patients	4 (67)	2 (20)	4 (40)	2 (22)	0 (0)	12 (26)
6 to 10 patients	2 (33)	1 (10)	0 (0)	6 (67)	1 (9)	10 (22)
11 to 20 patients	0 (0)	2 (20)	0 (0)	1 (11)	0 (0)	3 (7)
More than 20 patients	0 (0)	5 (50)	0 (0)	0 (0)	1 (9)	6 (13)
DME						
None	1 (17)	0 (0)	0 (0)	0 (0)	2 (18)	3 (7)
1 to 5 patients	1 (17)	0 (0)	4 (40)	1 (11)	3 (27)	9 (20)
6 to 10 patients	1 (17)	1 (10)	2 (20)	1 (11)	4 (36)	9 (20)
11 to 20 patients	1 (17)	1 (10)	2 (20)	1 (11)	1 (9)	6 (13)
More than 20 patients	2 (33)	8 (80)	2 (20)	6 (67)	1 (9)	19 (41)
Other indications						
None	5 (83)	7 (70)	6 (60)	1 (11)	10 (91)	29 (63)
1 to 5 patients	0 (0)	0 (0)	3 (30)	6 (67)	0 (0)	9 (20)
6 to 10 patients	0 (0)	1 (10)	0 (0)	1 (11)	0 (0)	2 (4)
11 to 20 patients	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	1 (2)
More than 20 patients	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
I'm not sure	1 (17)	1 (10)	1 (10)	0 (0)	1 (9)	4 (9)
How many anti-VEGF intravitreal injections do you administer on average each month? (Q29)						
Less than 5 per month	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	2 (4)
5 to 20 per month	0 (0)	0 (0)	0 (0)	2 (22)	2 (18)	4 (9)

Table 1. Physician Experience With Aflibercept, Overall and by Country

Question	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
21 to 40 per month	0 (0)	1 (10)	1 (10)	2 (22)	2 (18)	6 (13)
More than 40 per month	6 (100)	9 (90)	8 (80)	5 (56)	5 (45)	33 (72)
I don’t know	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	1 (2)
When did you last administer an Eylea injection? (Q30)						
Less than 1 month ago	6 (100)	10 (100)	10 (100)	9 (100)	9 (82)	44 (96)
1 to 3 months ago	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	2 (4)

[a]The pre-filled syringe option was not on the market at the time the survey was conducted

Table 2. Physician Characteristics, Overall and by Country

Question	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
What is your focus within ophthalmology? (Q28) Tick all that apply.						
Retina	6 (100)	10 (100)	10 (100)	9 (100)	11 (100)	46 (100)
General ophthalmology	2 (33)	7 (70)	2 (20)	1 (11)	1 (9)	13 (28)
Glaucoma	0 (0)	6 (60)	1 (10)	0 (0)	0 (0)	7 (15)
Cataract	1 (17)	7 (70)	4 (40)	0 (0)	2 (18)	14 (30)
Other	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	2 (4)
How many years have you been treating patients? (Q31)						
5 years or fewer	0 (0)	3 (30)	0 (0)	1 (11)	0 (0)	4 (9)
6 to 10 years	2 (33)	1 (10)	4 (40)	0 (0)	1 (9)	8 (17)
11 to 15 years	1 (17)	1 (10)	2 (20)	2 (22)	1 (9)	7 (15)
16 to 20 years	1 (17)	0 (0)	1 (10)	3 (33)	6 (55)	11 (24)
21 to 25 years	1 (17)	0 (0)	1 (10)	2 (22)	2 (18)	6 (13)
More than 25 years	1 (17)	5 (50)	2 (20)	1 (11)	1 (9)	10 (22)
Are you…? (Q32)						
Male	3 (50)	9 (90)	7 (70)	7 (78)	7 (64)	33 (72)
Female	3 (50)	1 (10)	3 (30)	2 (22)	4 (36)	13 (28)

Table 3-1. Physician Knowledge: Storage and Preparation, Overall and by Country

For each of the following statements related to the storage and preparation of Eylea, please indicate if the statement is true, not true, or if you do not know. (Q1)	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
Eylea is a suspension, which contains particulates and is cloudy						
Yes, this is true	1 (17)	0 (0)	0 (0)	0 (0)	1 (9)	2 (4)
No, this is not true*	5 (83) [36 - 100]	9 (90) [55 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	9 (82) [48 - 98]	42 (91) [79 - 98]
I don't know	0 (0)	1 (10)	0 (0)	0 (0)	1 (9)	2 (4)
For the intravitreal injection, a 30-gauge x ½ inch injection needle should be used						
Yes, this is true*	6 (100) [54 - 100]	8 (80) [44 - 97]	10 (100) [69 - 100]	9 (100) [66 - 100]	10 (91) [59 - 100]	43 (93) [82 - 99]
No, this is not true	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	1 (2)
I don't know	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	2 (4)
Adequate anaesthesia and asepsis (e.g., use of povidone iodine) must be provided for the patient						
Yes, this is true*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	10 (91) [59 - 100]	45 (98) [88 - 100]
No, this is not true	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	1 (2)
Number of correct responses selected among the three Yes/No questions listed above						
1	0 (0)	1 (10)	0 (0)	0 (0)	1 (9)	2 (4)
2	1 (17)	1 (10)	0 (0)	0 (0)	2 (18)	4 (9)
3	5 (83)	8 (80)	10 (100)	9 (100)	8 (73)	40 (87)
The next three questions were only asked of those physicians who indicated they use the vial						
Not applicable skip pattern	2	0	1	0	1	4
The vial of Eylea is reusable between patients and can be used for multiple injections						
No, this is not true*	4 (100) [40 - 100]	9 (90) [55 - 100]	9 (100) [66 - 100]	9 (100) [66 - 100]	10 (100) [69 - 100]	41 (98) [87 - 100]
No answer	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
The vial of Eylea must be stored in the refrigerator (2°C to 8°C)						
Yes, this is true*	4 (100) [40 - 100]	10 (100) [69 - 100]	8 (89) [52 - 100]	8 (89) [52 - 100]	7 (70) [35 - 93]	37 (88) [74 - 96]
No, this is not true	0 (0)	0 (0)	1 (11)	1 (11)	1 (10)	3 (7)
I don't know	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	2 (5)
Prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours						
Yes, this is true	2 (50)	4 (40)	4 (44)	1 (11)	1 (10)	12 (29)
No, this is not true*	0 (0) [0 - 60]	5 (50) [19 - 81]	5 (56) [21 - 86]	8 (89) [52 - 100]	7 (70) [35 - 93]	25 (60) [43 - 74]
I don't know	2 (50)	1 (10)	0 (0)	0 (0)	2 (20)	5 (12)
Number of correct responses selected among the three Yes/No questions listed above						
1	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	1 (2)
2	4 (100)	6 (60)	5 (56)	2 (22)	4 (40)	21 (50)
3	0 (0)	4 (40)	4 (44)	7 (78)	5 (50)	20 (48)

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
What is the recommended dose for Eylea? (Q2)						
12.5 microlitres (0.5 mg)	2 (33)	1 (10)	1 (10)	0 (0)	0 (0)	4 (9)
50 microlitres (2 mg)*	3 (50) [12 - 88]	9 (90) [55 - 100]	9 (90) [55 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	41 (89) [76 - 96]
100 microlitres (4 mg)	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
For each of the following statements related to the Eylea dosing and monitoring recommendations for the treatment of wAMD, please indicate if the statement is true, not true, or if you do not know. (Q3)						
During the first 12 months, treatment is initiated with one injection per month for three consecutive doses, followed by one injection every 2 months.						
Yes, this is true*	5 (83) [36 - 100]	9 (90) [55 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	44 (96) [85 - 99]
No, this is not true	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
I don't know	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
During the first 12 months, there is no requirement for monitoring between injections.						
Yes, this is true*	3 (50) [12 - 88]	2 (20) [3 - 56]	8 (80) [44 - 97]	2 (22) [3 - 60]	8 (73) [39 - 94]	23 (50) [35 - 65]
No, this is not true	3 (50)	8 (80)	2 (20)	7 (78)	2 (18)	22 (48)
I don't know	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	1 (2)
After the first 12 months, the treatment interval may be extended based on visual and anatomical outcomes.						
Yes, this is true*	6 (100) [54 - 100]	9 (90) [55 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	10 (91) [59 - 100]	44 (96) [85 - 99]
No, this is not true	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	1 (2)
I don't know	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
After the first 12 months, the schedule for monitoring should be determined by the treating physician and may be more frequent than the schedule of injections.						
Yes, this is true*	6 (100) [54 - 100]	10 (100) [69 - 100]	9 (90) [55 - 100]	9 (100) [66 - 100]	9 (82) [48 - 98]	43 (93) [82 - 99]
No, this is not true	0 (0)	0 (0)	1 (10)	0 (0)	2 (18)	3 (7)
Number of correct responses selected among the four Yes/No questions listed above						
1	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
2	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	2 (4)
3	4 (67)	7 (70)	3 (30)	7 (78)	2 (18)	23 (50)
4	2 (33)	2 (20)	7 (70)	2 (22)	7 (64)	20 (43)
For each of the following statements related to the Eylea dosing recommendations for the treatment of macular oedema secondary to CRVO or BRVO, please indicate if the statement is true, not true, or if you do not know. (Q4)						

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
Not applicable skip pattern (did not tick CRVO or BRVO in screener question 2)	0	1	4	1	1	7
After the initial injection, treatment is given monthly.						
Yes, this is true*	3 (50) [12 - 88]	6 (67) [30 - 93]	5 (83) [36 - 100]	5 (63) [24 - 91]	7 (70) [35 - 93]	26 (67) [50 - 81]
No, this is not true	3 (50)	3 (33)	1 (17)	3 (38)	3 (30)	13 (33)
The interval between two doses should not be shorter than 2 months.						
Yes, this is true	0 (0)	2 (22)	0 (0)	0 (0)	0 (0)	2 (5)
No, this is not true*	6 (100) [54 - 100]	7 (78) [40 - 97]	5 (83) [36 - 100]	8 (100) [63 - 100]	9 (90) [55 - 100]	35 (90) [76 - 97]
I don't know	0 (0)	0 (0)	1 (17)	0 (0)	1 (10)	2 (5)
If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued.						
Yes, this is true*	5 (83) [36 - 100]	9 (100) [66 - 100]	6 (100) [54 - 100]	6 (75) [35 - 97]	9 (90) [55 - 100]	35 (90) [76 - 97]
No, this is not true	1 (17)	0 (0)	0 (0)	2 (25)	0 (0)	3 (8)
I don't know	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	1 (3)
Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity.						
Yes, this is true*	5 (83) [36 - 100]	8 (89) [52 - 100]	6 (100) [54 - 100]	8 (100) [63 - 100]	10 (100) [69 - 100]	37 (95) [83 - 99]
No, this is not true	1 (17)	1 (11)	0 (0)	0 (0)	0 (0)	2 (5)
Number of correct responses selected among the four Yes/No questions listed above						
2	1 (17)	2 (22)	1 (17)	1 (13)	1 (10)	6 (15)
3	3 (50)	2 (22)	0 (0)	3 (38)	3 (30)	11 (28)
4	2 (33)	5 (56)	5 (83)	4 (50)	6 (60)	22 (56)
For each of the following statements related to the Eylea dosing recommendations for the treatment of DME, please indicate if the statement is true, not true, or if you do not know. (Q5)						
Not applicable skip pattern (did not tick DME in screener question 2)	1	1	2	0	1	5
Eylea treatment is initiated with one injection per month for five consecutive doses.						
Yes, this is true*	4 (80) [28 - 99]	9 (100) [66 - 100]	8 (100) [63 - 100]	8 (89) [52 - 100]	10 (100) [69 - 100]	39 (95) [83 - 99]
No, this is not true	1 (20)	0 (0)	0 (0)	1 (11)	0 (0)	2 (5)
After the first 5 months, Eylea treatment is followed by one injection every 2 months.						
Yes, this is true*	4 (80) [28 - 99]	8 (89) [52 - 100]	8 (100) [63 - 100]	9 (100) [66 - 100]	9 (90) [55 - 100]	38 (93) [80 - 98]
No, this is not true	1 (20)	0 (0)	0 (0)	0 (0)	1 (10)	2 (5)
I don't know	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	1 (2)

Table 3-2. Physician Knowledge: Dosing and Monitoring, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
During the first 12 months, there is no requirement for monitoring between injections.						
Yes, this is true*	1 (20) [1 - 72]	3 (33) [7 - 70]	7 (88) [47 - 100]	3 (33) [7 - 70]	4 (40) [12 - 74]	18 (44) [28 - 60]
No, this is not true	4 (80)	6 (67)	1 (13)	6 (67)	4 (40)	21 (51)
I don't know	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	2 (5)
Number of correct responses selected among the three Yes/No questions listed above						
0	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
1	0 (0)	1 (11)	0 (0)	1 (11)	1 (10)	3 (7)
2	3 (60)	5 (56)	1 (13)	5 (56)	5 (50)	19 (46)
3	1 (20)	3 (33)	7 (88)	3 (33)	4 (40)	18 (44)
The Eylea vial contains more than the recommended dose of Eylea and excess volume should be expelled before injecting. (Q8)						
True*	4 (100) [40 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	7 (78) [40 - 97]	10 (100) [69 - 100]	40 (95) [84 - 99]
False	0 (0)	0 (0)	0 (0)	2 (22)	0 (0)	2 (5)
Not applicable skip pattern	2	0	1	0	1	4
After removing all of the drug from the Eylea vial with a syringe, the plunger of the syringe should be depressed until the tip aligns with the line that marks which number of millilitres (ml) on the syringe? (Q9)						
0.05 ml*	4 (100) [40 - 100]	9 (90) [55 - 100]	9 (100) [66 - 100]	8 (89) [52 - 100]	10 (100) [69 - 100]	40 (95) [84 - 99]
0.1 ml	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	1 (2)
0.5 ml	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
Not applicable skip pattern	2	0	1	0	1	4

Table 3-3. Physician Knowledge: Safe Use, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
What should you do to prepare the patient before the start of treatment with Eylea? (Q10) Tick all that apply.						
Provide the Patient Booklet which includes a Patient Information Audio CD and Patient Information Leaflet*	4 (67) [22 - 96]	7 (70) [35 - 93]	9 (90) [55 - 100]	6 (67) [30 - 93]	10 (91) [59 - 100]	36 (78) [64 - 89]
Explain the implications of anti-VEGF treatment*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Inform the patient to report any signs and symptoms potentially associated with serious adverse events and provide information on when to seek medical attention*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Selected all three of the correct responses	4 (67) [22 - 96]	7 (70) [35 - 93]	9 (90) [55 - 100]	6 (67) [30 - 93]	10 (91) [59 - 100]	36 (78) [64 - 89]
Selected at least two of the three correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Selected at least one of the three correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Eylea is contraindicated in which of the following patients? (Q11) Tick all that apply.						
Patients with a known hypersensitivity to Eylea or to any of the excipients (e.g., non-active ingredients)*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Patients with active or suspected ocular or periocular infection*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Patients with high blood pressure	3 (50)	1 (10)	0 (0)	1 (11)	0 (0)	5 (11)
Patients with active severe intraocular inflammation*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Selected all three of the correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Selected at least two of the three correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Selected at least one of the three correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
What is the recommended use of Eylea in women of childbearing potential? (Q12) Tick all that apply.						
Women of childbearing potential must use effective contraception during treatment and for at least 1 month after the last Eylea injection	0 (0)	1 (10)	0 (0)	0 (0)	1 (9)	2 (4)
Women of childbearing potential must use effective contraception during treatment and for at least 3 months after the last Eylea injection*	6 (100) [54 - 100]	7 (70) [35 - 93]	10 (100) [69 - 100]	6 (67) [30 - 93]	7 (64) [31 - 89]	36 (78) [64 - 89]
Eylea should not be used in pregnancy unless the potential benefit outweighs the potential risk to the foetus*	3 (50) [12 - 88]	6 (60) [26 - 88]	5 (50) [19 - 81]	8 (89) [52 - 100]	9 (82) [48 - 98]	31 (67) [52 - 80]
Eylea should never be used in pregnancy	3 (50)	3 (30)	5 (50)	0 (0)	2 (18)	13 (28)
I don't know	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
Selected both of the correct responses	3 (50) [12 - 88]	4 (40) [12 - 74]	5 (50) [19 - 81]	5 (56) [21 - 86]	7 (64) [31 - 89]	24 (52) [37 - 67]
Selected at least one of the two correct responses	6 (100) [54 - 100]	9 (90) [55 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	9 (82) [48 - 98]	43 (93) [82 - 99]

Table 3-4. Physician Knowledge: Injection Procedure, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
Should topical anaesthesia be used prior to the Eylea injection? (Q13)						
Yes*	5 (83) [36 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	45 (98) [88 - 100]
No	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
A disinfectant (e.g., povidone iodine solution) should be applied to the periocular skin, eyelid, and ocular surface. (Q14)						
True*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	10 (91) [59 - 100]	45 (98) [88 - 100]
False	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	1 (2)
After the disinfectant is applied, which of the following steps should be taken prior to marking the scleral injection site? (Q15) Tick all that apply.						
Cover the eye with a sterile drape*	4 (67) [22 - 96]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	10 (91) [59 - 100]	43 (93) [82 - 99]
Insert a sterile lid speculum*	6 (100) [54 - 100]	10 (100) [69 - 100]	9 (90) [55 - 100]	8 (89) [52 - 100]	11 (100) [72 - 100]	44 (96) [85 - 99]
Dilate the eye	0 (0)	5 (50)	2 (20)	0 (0)	1 (9)	8 (17)
Selected both of the correct responses	4 (67) [22 - 96]	10 (100) [69 - 100]	9 (90) [55 - 100]	8 (89) [52 - 100]	10 (91) [59 - 100]	41 (89) [76 - 96]
Selected at least one of the two correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
In preparation for the Eylea injection, the eye should be marked at which of the following positions: (Q16)						
At a distance 3.0 to 3.5 mm posterior to the limbus	1 (17)	3 (30)	0 (0)	0 (0)	0 (0)	4 (9)
At a distance 3.5 to 4.0 mm posterior to the limbus*	5 (83) [36 - 100]	6 (60) [26 - 88]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	41 (89) [76 - 96]
At a distance 4.0 to 4.5 mm posterior to the limbus	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (2)
How should the injection needle be inserted into the eye? (Q17)						
Into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]

Table 3-5. Physician Knowledge: Side Effects, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
How should physicians evaluate a patient's vision immediately after an Eylea injection? (Q18)						
Using a standard eye chart (e.g., Snellen, Notation Monoyer, Letter Score, ETDRS, Decimal)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	1 (2)
By hand movements or counting fingers*	5 (83) [36 - 100]	8 (80) [44 - 97]	7 (70) [35 - 93]	6 (67) [30 - 93]	9 (82) [48 - 98]	35 (76) [61 - 87]
It is not necessary to evaluate a patient's vision immediately after an Eylea injection	0 (0)	2 (20)	2 (20)	3 (33)	2 (18)	9 (20)
None of the above	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)
An increase in intraocular pressure has been seen within 60 minutes after an injection with Eylea. (Q19)						
True*	5 (83) [36 - 100]	10 (100) [69 - 100]	8 (80) [44 - 97]	7 (78) [40 - 97]	9 (82) [48 - 98]	39 (85) [71 - 94]
False	0 (0)	0 (0)	1 (10)	1 (11)	1 (9)	3 (7)
I don't know	1 (17)	0 (0)	1 (10)	1 (11)	1 (9)	4 (9)
What should physicians do in relation to the potential of increased intraocular pressure immediately following an Eylea injection? (Q20) Tick all that apply.						
Ensure that sterile equipment is available to perform paracentesis if necessary*	5 (83) [36 - 100]	9 (90) [55 - 100]	8 (80) [44 - 97]	5 (56) [21 - 86]	11 (100) [72 - 100]	38 (83) [69 - 92]
Undertake appropriate monitoring if increased intraocular pressure is suspected (e.g., check for perfusion of the optic nerve head or tonometry)*	4 (67) [22 - 96]	9 (90) [55 - 100]	7 (70) [35 - 93]	8 (89) [52 - 100]	10 (91) [59 - 100]	38 (83) [69 - 92]
Nothing needs to be done because increased ocular pressure is normal and never harmful	1 (17)	0 (0)	2 (20)	0 (0)	0 (0)	3 (7)
Selected both of the correct responses	3 (50) [12 - 88]	8 (80) [44 - 97]	7 (70) [35 - 93]	4 (44) [14 - 79]	10 (91) [59 - 100]	32 (70) [54 - 82]
Selected at least one of the two correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	8 (80) [44 - 97]	9 (100) [66 - 100]	11 (100) [72 - 100]	44 (96) [85 - 99]
After the Eylea injection, patients should be instructed to report any symptoms suggestive of which of the following conditions? (Q21) Tick all that apply.						
Intraocular inflammation*	6 (100) [54 - 100]	10 (100) [69 - 100]	9 (90) [55 - 100]	8 (89) [52 - 100]	10 (91) [59 - 100]	43 (93) [82 - 99]
Drooping eyelid	0 (0)	2 (20)	7 (70)	2 (22)	3 (27)	14 (30)
Endophthalmitis*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Selected both of the correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	9 (90) [55 - 100]	8 (89) [52 - 100]	10 (91) [59 - 100]	43 (93) [82 - 99]
Selected at least one of the two correct responses	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	11 (100) [72 - 100]	46 (100) [92 - 100]
Which of the following signs or symptoms are known undesirable side effects of using Eylea? (Q22)						
Endophthalmitis						
Yes, this is an undesirable effect*	6 (100) [54 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	8 (89) [52 - 100]	10 (91) [59 - 100]	44 (96) [85 - 99]
No, this is not an undesirable effect	0 (0)	0 (0)	0 (0)	1 (11)	1 (9)	2 (4)
Transient increased intraocular pressure						
Yes, this is an undesirable effect*	5 (83) [36 - 100]	10 (100) [69 - 100]	10 (100) [69 - 100]	9 (100) [66 - 100]	10 (91) [59 - 100]	44 (96) [85 - 99]
No, this is not an undesirable effect	1 (17)	0 (0)	0 (0)	0 (0)	1 (9)	2 (4)
Fever						

Table 3-5. Physician Knowledge: Side Effects, Overall and by Country

Question	France (N = 6) n (%) [95% CI]	Germany (N = 10) n (%) [95% CI]	Italy (N = 10) n (%) [95% CI]	Spain (N = 9) n (%) [95% CI]	UK (N = 11) n (%) [95% CI]	Overall (N = 46) n (%) [95% CI]
Yes, this is an undesirable effect	2 (33)	2 (20)	1 (10)	0 (0)	0 (0)	5 (11)
No, this is not an undesirable effect*	3 (50) [12 - 88]	5 (50) [19 - 81]	7 (70) [35 - 93]	9 (100) [66 - 100]	10 (91) [59 - 100]	34 (74) [59 - 86]
I don't know	1 (17)	3 (30)	1 (10)	0 (0)	1 (9)	6 (13)
No answer	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	1 (2)
Cataract (traumatic, nuclear, subcapsular, cortical) or lenticular opacities						
Yes, this is an undesirable effect*	6 (100) [54 - 100]	8 (80) [44 - 97]	9 (90) [55 - 100]	8 (89) [52 - 100]	10 (91) [59 - 100]	41 (89) [76 - 96]
No, this is not an undesirable effect	0 (0)	2 (20)	1 (10)	1 (11)	1 (9)	5 (11)
Tear or detachment of the retinal pigment epithelium						
Yes, this is an undesirable effect*	5 (83) [36 - 100]	8 (80) [44 - 97]	9 (90) [55 - 100]	8 (89) [52 - 100]	9 (82) [48 - 98]	39 (85) [71 - 94]
No, this is not an undesirable effect	1 (17)	2 (20)	1 (10)	1 (11)	2 (18)	7 (15)
Headache						
Yes, this is an undesirable effect	4 (67)	5 (50)	1 (10)	5 (56)	0 (0)	15 (33)
No, this is not an undesirable effect*	1 (17) [0 - 64]	3 (30) [7 - 65]	7 (70) [35 - 93]	4 (44) [14 - 79]	10 (91) [59 - 100]	25 (54) [39 - 69]
I don't know	1 (17)	2 (20)	2 (20)	0 (0)	1 (9)	6 (13)

Table 4. Physician Receipt and Use of Aflibercept Educational Materials, Overall and by Country

Please indicate whether you have received and/or reviewed the following Eylea informational material. (Q23)	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
Summary of Product Characteristics						
Have you received the material?						
Yes	5 (83)	10 (100)	9 (90)	8 (89)	11 (100)	43 (93)
No	1 (17)	0 (0)	1 (10)	1 (11)	0 (0)	3 (7)
Have you reviewed the material?						
Yes	5 (100)	9 (90)	9 (100)	8 (100)	10 (91)	41 (95)
No	0 (0)	1 (10)	0 (0)	0 (0)	1 (9)	2 (5)
Not applicable skip pattern (did not receive this material)	1	0	1	1	0	3
Eylea Prescriber Guide						
Have you received the material?						
Yes	6 (100)	10 (100)	9 (90)	6 (67)	9 (82)	40 (87)
No	0 (0)	0 (0)	1 (10)	3 (33)	2 (18)	6 (13)
Have you reviewed the material?						
Yes	5 (83)	10 (100)	9 (100)	6 (100)	9 (100)	39 (98)
No	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)
Not applicable skip pattern (did not receive this material)	0	0	1	3	2	6
Intravitreal injection procedure video						
Have you received the material?						
Yes	4 (67)	8 (80)	4 (40)	6 (67)	8 (73)	30 (65)
No	2 (33)	2 (20)	6 (60)	3 (33)	3 (27)	16 (35)
Have you reviewed the material?						
Yes	3 (75)	7 (88)	4 (100)	6 (100)	4 (50)	24 (80)
No	1 (25)	1 (13)	0 (0)	0 (0)	4 (50)	6 (20)
Not applicable skip pattern (did not receive this material)	2	2	6	3	3	16
Patient Booklet including a Patient Information Audio CD and the Patient Information Leaflet						
Have you received the material?						
Yes	5 (83)	8 (80)	8 (80)	5 (56)	11 (100)	37 (80)

Table 4. Physician Receipt and Use of Aflibercept Educational Materials, Overall and by Country

Please indicate whether you have received and/or reviewed the following Eylea informational material. (Q23)	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
No	1 (17)	2 (20)	2 (20)	4 (44)	0 (0)	9 (20)
Have you reviewed the material?						
Yes	3 (60)	6 (75)	8 (100)	4 (80)	7 (64)	28 (76)
No	2 (40)	2 (25)	0 (0)	1 (20)	4 (36)	9 (24)
Not applicable skip pattern (did not receive this material)	1	2	2	4	0	9

Table 5. Physician Ratings of Aflibercept Educational Materials, Overall and by Country

How helpful were these materials to you in treating and educating your patients? (Q24) [a]	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
Summary of Product Characteristics						
1 - Not at all helpful	0 (0)	0 (0)	1 (11)	0 (0)	2 (18)	3 (7)
2	2 (40)	2 (20)	2 (22)	0 (0)	1 (9)	7 (16)
3	2 (40)	1 (10)	3 (33)	7 (88)	5 (45)	18 (42)
4 - Extremely helpful	1 (20)	7 (70)	3 (33)	1 (13)	3 (27)	15 (35)
Not applicable skip pattern (did not receive this material)	1	0	1	1	0	3
Eylea Prescriber Guide						
1 - Not at all helpful	2 (33)	1 (10)	1 (11)	0 (0)	0 (0)	4 (10)
2	1 (17)	2 (20)	2 (22)	1 (17)	2 (22)	8 (20)
3	2 (33)	1 (10)	4 (44)	3 (50)	6 (67)	16 (40)
4 - Extremely helpful	1 (17)	6 (60)	2 (22)	2 (33)	1 (11)	12 (30)
Not applicable skip pattern (did not receive this material)	0	0	1	3	2	6
Intravitreal injection procedure video						
1 - Not at all helpful	1 (25)	1 (13)	1 (25)	1 (17)	3 (38)	7 (23)
2	1 (25)	2 (25)	2 (50)	2 (33)	1 (13)	8 (27)
3	2 (50)	4 (50)	1 (25)	2 (33)	4 (50)	13 (43)
4 - Extremely helpful	0 (0)	1 (13)	0 (0)	1 (17)	0 (0)	2 (7)
Not applicable skip pattern (did not receive this material)	2	2	6	3	3	16
Patient Booklet						
1 - Not at all helpful	1 (20)	1 (13)	0 (0)	0 (0)	2 (18)	4 (11)
2	0 (0)	2 (25)	0 (0)	1 (20)	0 (0)	3 (8)
3	4 (80)	4 (50)	4 (50)	3 (60)	5 (45)	20 (54)
4 - Extremely helpful	0 (0)	1 (13)	4 (50)	1 (20)	4 (36)	10 (27)
Not applicable skip pattern (did not receive this material)	1	2	2	4	0	9
Patient Information Audio CD						
1 - Not at all helpful	1 (20)	1 (13)	0 (0)	0 (0)	3 (27)	5 (14)
2	1 (20)	3 (38)	2 (25)	2 (40)	1 (9)	9 (24)
3	3 (60)	3 (38)	5 (63)	2 (40)	4 (36)	17 (46)
4 - Extremely helpful	0 (0)	1 (13)	1 (13)	1 (20)	3 (27)	6 (16)
Not applicable skip pattern (did not receive this material)	1	2	2	4	0	9
Patient Information Leaflet						

Table 5. Physician Ratings of Aflibercept Educational Materials, Overall and by Country

How helpful were these materials to you in treating and educating your patients? (Q24) [a]	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
1 - Not at all helpful	1 (20)	0 (0)	0 (0)	0 (0)	2 (18)	3 (8)
2	0 (0)	3 (38)	0 (0)	2 (40)	0 (0)	5 (14)
3	4 (80)	1 (13)	5 (63)	2 (40)	4 (36)	16 (43)
4 - Extremely helpful	0 (0)	4 (50)	3 (38)	1 (20)	5 (45)	13 (35)
Not applicable skip pattern (did not receive this	1	2	2	4	0	9

Table 6. Physician Use of Patient Booklet, Overall and by Country

Question	France (N = 6) n (%)	Germany (N = 10) n (%)	Italy (N = 10) n (%)	Spain (N = 9) n (%)	UK (N = 11) n (%)	Overall (N = 46) n (%)
Considering the patients under your care who are receiving Eylea injections, to how many did you provide a Patient Booklet? (Q26)						
All of my patients	0 (0)	1 (10)	3 (30)	1 (11)	3 (27)	8 (17)
Most of my patients	0 (0)	5 (50)	5 (50)	1 (11)	4 (36)	15 (33)
A few of my patients	4 (67)	3 (30)	1 (10)	3 (33)	2 (18)	13 (28)
None of my patients	2 (33)	1 (10)	1 (10)	4 (44)	2 (18)	10 (22)
When would you provide the Patient Booklet and discuss it with your patient? (Q27) Tick all that apply.						
Before the start of treatment with Eylea	3 (75)	7 (78)	9 (100)	4 (80)	9 (100)	32 (89)
I do not reference the Patient Information Booklet	1 (25)	2 (22)	0 (0)	1 (20)	0 (0)	4 (11)
Not applicable skip pattern (selected "None of my patients" for Q26)	2	1	1	4	2	10

Annex 10. Patient Analysis Tables Stratified by Physician Knowledge Tertile

Tables

Table 2. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Physician Knowledge

Question	Physician Knowledge		
	Lowest Tertile (N = 273) n (%)	Middle Tertile (N = 255) n (%)	Highest Tertile (N = 245) n (%)
Which of the following issues or health conditions should you tell your ophthalmologist about before you have an Eylea injection? (Q1)			
Any current eye problems (for example, infection, pain or redness in the eye)			
Yes*	245 (90)	229 (90)	236 (96)
No	24 (9)	18 (7)	8 (3)
I don't know	4 (1)	8 (3)	1 (0)
Any allergies to medications (for example, iodine or painkillers)			
Yes*	247 (90)	218 (85)	230 (94)
No	21 (8)	26 (10)	9 (4)
I don't know	5 (2)	11 (4)	6 (2)
Any problems with eye injections in the past			
Yes*	247 (90)	218 (85)	225 (92)
No	22 (8)	27 (11)	12 (5)
I don't know	4 (1)	10 (4)	7 (3)
No answer	0 (0)	0 (0)	1 (0)
If you have glaucoma or have had issues with feeling of high pressure in the eye in the past			
Yes*	243 (89)	196 (77)	227 (93)
No	15 (5)	36 (14)	11 (4)
I don't know	15 (5)	23 (9)	6 (2)
No answer	0 (0)	0 (0)	1 (0)

Table 2. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Physician Knowledge

Question	Physician Knowledge		
	Lowest Tertile (N = 273) n (%)	Middle Tertile (N = 255) n (%)	Highest Tertile (N = 245) n (%)
If you see flashes of light			
Yes*	241 (88)	214 (84)	222 (91)
No	22 (8)	31 (12)	11 (4)
I don't know	10 (4)	10 (4)	11 (4)
No answer	0 (0)	0 (0)	1 (0)
If you see moving spots (known as floaters) in your eye			
Yes*	242 (89)	216 (85)	215 (88)
No	20 (7)	30 (12)	23 (9)
I don't know	11 (4)	9 (4)	6 (2)
No answer	0 (0)	0 (0)	1 (0)
Any medications that you have used			
Yes*	232 (85)	208 (82)	215 (88)
No	33 (12)	22 (9)	19 (8)
I don't know	8 (3)	25 (10)	11 (4)
If you have had (or are going to have) an eye operation in the 4 weeks before or after the Eylea injection			
Yes*	245 (90)	215 (84)	222 (91)
No	19 (7)	32 (13)	16 (7)
I don't know	9 (3)	8 (3)	7 (3)
If you are pregnant, are planning to become pregnant, or are breastfeeding			
Yes*	124 (45)	115 (45)	160 (65)
No	92 (34)	83 (33)	45 (18)
I don't know	51 (19)	53 (21)	36 (15)
No answer	6 (2)	4 (2)	4 (2)

Table 2. Patient Knowledge: Health Conditions to Discuss With Doctor Prior to Injection, by Physician Knowledge

Question	Physician Knowledge		
	Lowest Tertile (N = 273) n (%)	Middle Tertile (N = 255) n (%)	Highest Tertile (N = 245) n (%)
Number of correct responses selected among the nine Yes/No questions listed above			
0	0 (0)	5 (2)	0 (0)
1	0 (0)	4 (2)	3 (1)
2	6 (2)	5 (2)	0 (0)
3	4 (1)	6 (2)	4 (2)
4	10 (4)	9 (4)	5 (2)
5	12 (4)	13 (5)	8 (3)
6	15 (5)	28 (11)	15 (6)
7	44 (16)	40 (16)	16 (7)
8	94 (34)	57 (22)	71 (29)
9	88 (32)	88 (35)	123 (50)

Table 3. Patient Knowledge: Possible Side Effects, by Physician Knowledge

	Physician Knowledge		
Question	**Lowest Tertile (N = 273) n (%)**	**Middle Tertile (N = 255) n (%)**	**Highest Tertile (N = 245) n (%)**
We are interested in finding out what you know about possible side effects that a person can have with Eylea. We do NOT want to know about your own personal experiences. Is […side-effect] possible side effect of Eylea? (Q2)			
...a red or bloodshot eye			
Yes*	181 (66)	167 (65)	195 (80)
No	66 (24)	53 (21)	25 (10)
I don't know	26 (10)	35 (14)	25 (10)
...nausea and vomiting (feeling or being sick)			
Yes	77 (28)	66 (26)	85 (35)
No*	161 (59)	143 (56)	107 (44)
I don't know	35 (13)	46 (18)	53 (22)
...eye pain			
Yes*	189 (69)	182 (71)	198 (81)
No	73 (27)	49 (19)	38 (16)
I don't know	11 (4)	24 (9)	9 (4)
...detachment of the gel-like substance inside the eye from the retina			
Yes*	98 (36)	103 (40)	124 (51)
No	90 (33)	73 (29)	55 (22)
I don't know	85 (31)	79 (31)	66 (27)
...seeing halos around lights			
Yes*	112 (57)	113 (51)	124 (62)
No	54 (28)	69 (31)	47 (24)
I don't know	30 (15)	38 (17)	28 (14)
Not applicable, this was not asked in Germany	77	35	46

Table 3. Patient Knowledge: Possible Side Effects, by Physician Knowledge

Question	Physician Knowledge		
	Lowest Tertile (N = 273) n (%)	Middle Tertile (N = 255) n (%)	Highest Tertile (N = 245) n (%)
...sudden flashes of light			
Yes*	131 (48)	131 (51)	151 (62)
No	97 (36)	86 (34)	52 (21)
I don't know	45 (16)	38 (15)	42 (17)
...sudden appearance or increase in moving spots (known as floaters)			
Yes*	185 (68)	162 (64)	182 (74)
No	68 (25)	59 (23)	37 (15)
I don't know	20 (7)	34 (13)	26 (11)
...cloudy or blurred vision			
Yes*	204 (75)	172 (67)	190 (78)
No	53 (19)	53 (21)	34 (14)
I don't know	16 (6)	30 (12)	21 (9)
...sensitivity to light			
Yes*	188 (69)	152 (60)	178 (73)
No	64 (23)	66 (26)	40 (16)
I don't know	21 (8)	37 (15)	27 (11)
...an eye infection			
Yes*	149 (55)	140 (55)	184 (75)
No	97 (36)	77 (30)	36 (15)
I don't know	27 (10)	38 (15)	25 (10)

Table 3. Patient Knowledge: Possible Side Effects, by Physician Knowledge

Question	Physician Knowledge		
	Lowest Tertile (N = 273) n (%)	Middle Tertile (N = 255) n (%)	Highest Tertile (N = 245) n (%)
Number of correct responses selected among the ten Yes/No questions listed above			
0	1 (0)	7 (3)	3 (1)
1	18 (7)	14 (5)	10 (4)
2	11 (4)	15 (6)	5 (2)
3	27 (10)	23 (9)	15 (6)
4	32 (12)	16 (6)	21 (9)
5	30 (11)	35 (14)	17 (7)
6	32 (12)	30 (12)	29 (12)
7	32 (12)	40 (16)	23 (9)
8	38 (14)	27 (11)	46 (19)
9	41 (15)	43 (17)	64 (26)
10	11 (4)	5 (2)	12 (5)

Table 4. Patient Knowledge: Appropriate Action in Response to Side Effects, by Physician Knowledge

	Physician Knowledge		
What should you do if you think you might be having a side effect from your Eylea injection? (Q3)	**Lowest Tertile (N = 273) n (%)**	**Middle Tertile (N = 255) n (%)**	**Highest Tertile (N = 245) n (%)**
Speak to your ophthalmologist (or someone in his or her office) immediately*	208 (76)	195 (76)	201 (82)
Wait 48 hours to see if the symptoms improve	56 (21)	45 (18)	39 (16)
None of the above	2 (1)	10 (4)	5 (2)
I don't know	7 (3)	5 (2)	0 (0)