NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: An Active Surveillance, Post-Authorization Safety Study (PASS) to Estimate Incidence Rates of Serious Infection, Malignancy, Cardiovascular (CV) and Other Safety Events of Interest Among all Patients Treated with Ruxience for Rheumatoid Arthritis (RA) Within the Swedish, Population-based, Anti-Rheumatic Treatment in Sweden (ARTIS) Register

Date: 17 July 2024

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Keywords: rheumatoid arthritis, active surveillance, ARTIS register, infectious diseases, malignancy, cardiovascular events, Sweden

Rationale and background: Approved in the European Union (EU) on 01 April 2020, PF-05280586 (Ruxience) was developed by Pfizer as a biosimilar to the licensed reference product, MabThera. Pfizer proposed the assessment of safety events of special interest based on the Ruxience EU Risk Management Plan (RMP) version 1.0 ((infections including serious infections (Important Identified Risk), malignancies (Important Potential Risk), impact on cardiovascular disease (CVD) (Important Potential Risk) and use in pregnancy (Missing Information)).[1] This study was designated as a Post-Authorization Safety Study (PASS) and was conducted voluntarily by Pfizer as a "Category 4 Additional Pharmacovigilance Activities" in line with the reference product.

Research question: What are the incidence rates of safety events of special interest in patients with RA who are enrolled in ARTIS and initiate treatment with Ruxience?

Objectives: To estimate incidence rates of infections, including serious infections, malignancies, cardiovascular events, and use during pregnancy among all patients with rheumatoid arthritis in the ARTIS register who initiate Ruxience.

Study design: This non-interventional, active surveillance study used data from the established ARTIS register, an ongoing, prospective, disease based cohort started in 1999.

Setting: Mandated by the Swedish Society of Rheumatology, ARTIS is a research project hosted by the Karolinska Institutet. Since 1999, ARTIS has conducted a safety surveillance programme for immunomodulators based on the Swedish Rheumatology Quality (SRQ) register linked to additional registers and includes all presently available biologics used for the treatment of patients with inflammatory rheumatic diseases. It covers approximately 90% of all biologic initiations in Sweden after 1999.[2]

[1] Ruxience (rituximab) European Union Risk Management Plan Version 1.0 dated December 2019. ruxience-epar-risk-management-plan-summary_en.pdf (europa.eu)

[2] Wadstrom H, Eriksson J, Neovius M, et al. How good is the coverage and how accurate are exposure data in the Swedish Biologics Register (ARTIS)? Scand J Rheumatol 2015;44(1):22-8

Patients and study size, including dropouts: The study population consisted of all persons enrolled within the ARTIS register with at least 18 years of age at the time of enrollment who were diagnosed with RA by a rheumatologist and initiated treatment with Ruxience during the study period beginning with the first Ruxience initiator through 31 December 2023.

Variables and data sources: This study utilized data routinely captured in the ARTIS register, which included baseline patient characteristics (i.e., demographic and clinical characteristics, comorbidities and current and past therapies), and safety events of special interest including serious infections, all malignancies, CVD events, and use during pregnancy. Infectious and cardiovascular events were ascertained through record linkage with the Swedish Patient Register, which collects information on all hospitalised patients, and all visits to non-primary outpatient care. Malignancies were ascertained through linkage with the Swedish Cancer Register which contains data on date of cancer diagnosis and type of cancer according to the International Classification of Disease (ICD). Use in pregnancy was assessed through additional linkage with the Medical Birth Register which contains data from antenatal, obstetric, and neonatal records, and covers all live and still births (but not all miscarriages) in Sweden. Analysis included incidence rates and 95% confidence intervals of safety events of interest in Ruxience-exposed persons. No comparative analyses were planned.

Results: Note: Due to data linkage delays of one year or longer by the Swedish National Board of Health and Welfare, only data up through 31 December 2022 were available for analysis. Twenty-five patients initiated Ruxience in ARTIS between the first availability of Ruxience in Sweden in 2020 through 31 December 2022. Of these, 12 patients were observed prior to 31 December 2021, and were thus included in the analyses for malignancy outcomes (for which data were only available through 31 December 2021). The median age of Ruxience initiators was 66 years, and the majority were female (68%). The majority had RA disease for a lengthy period prior to Ruxience initiation with a median disease duration of 17.5 years. The majority of initiators had received 1-2 previous b/tsDMARDs (60%). A fifth (20%) had a previous cancer diagnosis and 24% had a history of joint surgery. No safety events of special interest were reported during follow-up among the Ruxience initiators. There were no deliveries recorded where Ruxience was started either before the delivery or where the drug was discontinued after the pregnancy was initiated.

Discussion:. This report describes the uptake of Ruxience in the treatment of RA since its availability in 2020 and any recorded safety events of special interest up to 31 December 2022 (31 December 2021 for malignancy outcomes) as recorded in ARTIS. No safety events of special interest were reported during follow-up among the Ruxience initiators. However, due to the very limited uptake of Ruxience in Sweden (n=25), no conclusions can be drawn from this study.

Marketing Authorization Holder(s): Pfizer, Inc

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Document Approval Record

Document Name:	B3281013 ARTIS Final Study Report Abstract 17JUL2024
Document Title:	B3281013 RUXIENCE FINAL STUDY REPPORT ABSTRACT 17JUL2024

Signed By:	Date(GMT)	Signing Capacity
Younus, Muhammad	17-Jul-2024 17:24:11	Final Approval
De Bernardi, Barbara	22-Jul-2024 18:11:36	EUQPPV Approval