4.0 Abstract

Title:

Drug utilisation study of upadacitinib (Rinvoq™) in Europe to evaluate the effectiveness of additional risk minimisation measures

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Rationale and Background:

Upadacitinib (Rinvoq™) is a selective and reversible inhibitor of JAK1 that was approved in Europe on 16 December 2019 for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). As with other JAK inhibitors already marketed in Europe, important safety risks have been identified with upadacitinib that require additional risk minimization measures (aRMMs). Using data derived from European RA registries, AbbVie plans to implement a drug utilisation study to characterise the use of upadacitinib (Rinvoq™) and evaluate the effectiveness of the aRMMs (HCP educational brochure and patient alert card [PAC]).

Research Question and Objectives:

This study aims to characterise the use of upadacitinib (Rinvoq™) in routine clinical care, including describing baseline characteristics of individuals with rheumatoid arthritis exposed to upadacitinib relative to individuals with rheumatoid arthritis exposed to other systemic treatments. This study also aims to evaluate the effectiveness of additional risk minimisation measures, including to 1) quantify the occurrence of upadacitinib use among patients who are at high risk for experiencing a venous thromboembolism (VTE) and among patients who are currently being treated for active tuberculosis, 2) quantify the number of patients who are pregnant at the time of initiation or become pregnant while taking upadacitinib, and 3) describe prescribing physicians' adherence to recommendations for patient screening and laboratory monitoring.

Study Design:

This will be a population-based cohort study of new users of upadacitinib (Rinvoq™) and selected bDMARDs marketed for the treatment of rheumatoid arthritis in Europe.

Population:

This study includes patients diagnosed with RA who are enrolled in one of five European RA registries ARTIS, DANBIO, BSRBR-RA, BIOBADASER, and RABBIT and initiate upadacitinib or a selected bDMARD comparator drug.

Variables:

Exposure: Each registry assigns drug exposure time to an exposure cohort based on medication classification (Table 2). Exposure is reported by the physician at enrolment into each registry; however, cohort definitions vary across the registries (Table 3). Changes to exposure are reported by the physician at follow-up visits. In ARTIS, registry data are combined with data on prescription medication from national registries to assign exposure. The upadacitinib cohort will include patients with RA initiating treatment with upadacitinib. The comparator bDMARD cohort will include patients with RA initiating a bDMARD treatment, except for BSRBR-RA, in which the comparator cohort is more specifically an anti-TNFα cohort of patients with RA initiating anti-TNFα therapy (defined as originator etanercept, infliximab or adalimumab only and biologic naïve at registration. This is a specified cohort designed for the purpose of comparison with newer agents.

Outcomes: The European RA registries collect information related to disease duration, severity, and treatment. Variables routinely collected by each registry (or captured via linkage to national registries), including patient demographics, comorbidities, and concomitant medications, will be included in this study to characterise individuals with RA using upadacitinib in routine clinical care relative to individuals exposed to other systemic treatments (i.e., bDMARDs). Additional outcomes will be described for patients

treated with upadacitinib to assess the effectiveness of additional risk minimization activities.

Data Sources:

This study will use data routinely collected by five European RA registries (ARTIS, DANBIO, BSRBR-RA, BIOBADASER, and RABBIT) or captured via linkage of RA patient data to nationwide health registers. These RA registries provide high-quality, longitudinal data capture of adult patients being treated with approved anti-rheumatic treatments.

Study Size:

The number of patients in the upadacitinib and comparator cohorts will vary between the registries. All initiators of upadacitinib or a selected bDMARD comparator treatment enrolled in one of five European RA registries during the study period will be included in the analysis. Based on available data, it is expected that the final report will include up to 1,000 upadacitinib new users each in ARTIS and DANBIO, and up to 400 upadacitinib new users in RABBIT. Patient enrolment estimates for BSRBR-RA and BIOBADASER are currently unknown.

Data Analysis:

All analyses will be descriptive; no statistical tests will be performed. Analyses will be performed separately for each registry and exposure group (i.e., upadacitinib cohort and selected bDMARD cohort). Baseline patient characteristics will be assessed at study drug initiation. To address important safety information communicated in the healthcare professional educational material and patient alert card, outcome indicators at the time of initiation will be evaluated in the upadacitinib cohort. Additional outcome indicators will be assessed in the upadacitinib cohort during their continuous treatment.

Milestones:

AbbVie will initiate the study upon endorsement of the study protocol by the EMA. Study progress will be reported in 2022 and 2023, and the final study report will be submitted to the EMA in September 2024.

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