PASS information

Title	Comparative Cohort Study of Long-term Safety Outcomes of Risankizumab Compared to Biologic Treatments for Ulcerative Colitis and Crohn's Disease in a Real-world Setting in Sweden and Denmark
Protocol version identifier	Version 3.1
Date of last version of protocol	30 January 2025
EU PAS register number	EUPAS1000000151
Active substance	Risankizumab (ATC code L04AC18)
Medicinal product	Skyrizi®
Product reference	EMEA/H/C/004759
Procedure number	Not applicable
Marketing authorisation holder(s)	EU: AbbVie Deutschland GmbH & Co. KG US: AbbVie Inc.
Joint PASS	No
Research question and objectives	The objective is to estimate and compare, where possible, the incidence rates of malignancy excluding non-melanoma skin cancer, non-melanoma skin cancer, serious infections (including opportunistic infections), serious hypersensitivity reactions and major adverse cardiovascular events, among individuals with moderate to severe ulcerative colitis and Crohn's disease aged ≥18 years who initiate risankizumab in the course of routine clinical care, as well as the incidence rates in individuals who initiate other approved biologic comparator treatments for the treatment of ulcerative colitis and Crohn's disease.
Country(-ies) of study	Denmark, Sweden

Abstract

Rationale and background

Ulcerative colitis (UC) and Crohn's disease (CD) are chronic relapsing, remitting inflammatory diseases of the gastrointestinal tract, grouped together as inflammatory bowel disease (IBD). Risankizumab is a humanized immunoglobulin G1 monoclonal antibody that targets the p19 subunit of the human cytokine interleukin-23, currently approved for the treatment of adult patients with moderately to severely active UC or CD who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy. Although the risankizumab clinical trials provide valuable information on the product's efficacy and safety, long-term safety data are needed for individuals who are exposed to risankizumab. A prospective population-based cohort study of individuals in routine clinical practice will be conducted to investigate the incidence and occurrence of safety outcomes including malignancy excluding non-melanoma skin cancer (NMSC), NMSC, serious infections (including opportunistic infections [OI]), serious hypersensitivity reactions, and major adverse cardiovascular events (MACE).

Research question and objective

The objective is to estimate and compare, where possible, the incidence rates of malignancy excluding NMSC, NMSC, serious infections (including OI), serious hypersensitivity reactions and MACE, among individuals with moderate to severe UC or CD aged ≥18 years who initiate risankizumab in the course of routine clinical care, as well as the incidence rates in individuals who initiate other approved biologic comparator treatments for the treatment of UC or CD at the same line of therapy.

Study design

This observational cohort population-based study will be carried out using linked data from the [redacted] Danish and Swedish national registers. A new-user, active comparator design will be used to assess the association between exposure to risankizumab or other approved biologic treatment, with each safety outcome of interest.

Population

The *study population* will be all adult individuals residing in Sweden or Denmark with moderate to severe UC or CD that receive treatment with risankizumab or one of the biologic comparator treatments according to information [redacted] between Q4 2022 and Q4 2032.

Variables

Main exposure of interest will be risankizumab compared to other approved biologic comparator treatments for the treatment of UC and CD. The safety outcomes will be malignancy excluding NMSC, NMSC, serious infections (including OI), serious hypersensitivity reactions and MACE. Incident malignancy will be identified via the linked national cancer registers in each country. The other outcomes will be captured [redacted]
Covariates such as comorbidities and previous and concomitant drug therapies will be retrieved [redacted]. Information on age, sex, region of residency, and education will be retrieved from the population registers.

Data sources

Linked data from the national health and population registers in Denmark and Sweden. Data from the IBD quality register in Sweden will also be used.

Study size

The study size will depend on the market uptake of risankizumab for UC and CD in Denmark and Sweden. All eligible individuals exposed to risankizumab identified through the data sources will be included, and no upper limit of the study size is defined. [redacted] The study size assessment is based on the probability that the upper limit of the confidence interval for the rate ratio stays below a level of concern. To reach the number of person-years for risankizumab needed for the upper confidence limit for the rate ratios for all outcomes to be under 2 (small effect size) with 90% probability, [redacted]

Data analysis

Appropriate statistical analyses in an active-comparator design will be used. Cox proportional hazards regression model will be used to evaluate the association between the exposure and each one of the safety outcomes. Crude and adjusted hazard ratios, using Inverse Probability of the Treatment Weighting, will be estimated. [redacted]

Milestones

An interim report of study results will be submitted to the EMA in Q4 2029. Progress reports will be submitted with the periodic safety update reports (PSUR) except for the year of interim report. The final study report will be submitted to the EMA in Q4 2034.