NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: Canadian Non-Interventional Study of Xeljanz in Rheumatoid Arthritis (CANTORAL)

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- **Rationale and background**

First-line Rheumatoid Arthritis (RA) therapy comprises a conventional synthetic (cs) disease-modifying antirheumatic drug (DMARD) as monotherapy or combination therapy. Addition of a biologic (b)DMARD or targeted synthetic (ts)DMARD is recommended for patients who do not achieve sufficient response with csDMARDs. Tofacitinib is an oral Janus kinase (JAK) inhibitor (tsDMARD) for the treatment of RA.

Although there are several studies for the assessment of efficacy (including patient reported outcomes) and safety of tofacitinib compared with placebo or methotrexate in the treatment of RA, there is limited information on its use in current practice in Canada. Specific questions still exist around the patients treated with tofacitinib, the clinical effectiveness of tofacitinib, and the persistence of tofacitinib. Studies focusing on these areas using real world data without interventions, are of great importance for payers, physicians, and patients in Canada.

- **Research question and objectives**

Primary objectives:

- To describe the profile of RA patients initiating treatment with tofacitinib in the Canadian real – world/clinical setting.

- To describe the clinical effectiveness of tofacitinib over time in patients with moderate to severe RA in the real-world/clinical setting.

Secondary objectives:

In patients with moderate to severe RA that are initiated on treatment with tofacitinib to:

- Describe treatment patterns and treatment trajectory.

- Describe adherence to treatment and its association with clinical effectiveness.

- Identify determinants of therapeutic response.

- Describe durability of response, persistence of treatment and reasons for discontinuation.

- Describe the change in patient-reported pain, fatigue, quality of life and health care resource utilization.

- Describe the incidence of adverse events (including serious adverse events) and AEs of special interest for tofacitinib (Major Adverse Cardiovascular Events (MACE), venous thromboembolism, malignancy (excluding Non-Melanoma Skin Cancer [NMSC]), NMSC, serious infections (ie, infections requiring hospitalization), and herpes zoster (serious and non-serious), gastrointestinal perforation, and hepatic events).

Exploratory Objective:

To describe profile, clinical effectiveness and safety in RA patients who are ≥50 years of age with one or more additional CV risk factors (CV+), as well as in patients who do not meet CV+ criteria (non-CV+).

- **Study design**

This will be an observational (non–interventional), multi-centre study using a prospective cohort design. Patients with moderate to severe RA that are newly treated with tofacitinib as per the decision of their physician, in accordance with the Canadian label.

- **Population**

RA Canadian patients treated as per standard of care.

- **Variables**

Outcomes

Information reported by patients (*Patient Reported Outcomes* [PRO]) and physicians on disease activity, functional status, quality of life and work productivity.

Frequency of adverse events of special interest.

- **Data sources**

Patients, through application of PROs:

- Patient global assessment.
- *Routine Assessment of Patients Index Data* (RAPID3): Disease activity.
- *Health Assessment Questionnaire* (HAQ): Functional status.
- *EuroQol Questionnaire* (EQ-5D): Quality of life.
- *Work Productivity and Activity Impairment* (WPAI): Work productivity.
- Spontaneously reported safety information.
- Medical records
- Clinical and demographic information of patients: age, sex, comorbidities, concomitant medications, risk factors.
- Characteristics of the disease: duration of the disease, laboratory test data, disease activity.
- Treatment: previous and current treatment alongside reason for discontinuation of previous treatment.

- **Study size**

500.

- **Data analysis**

The information collected by the Clinical Research Organization (CRO) will be analyzed through a statistical management plan. Initially, the sample will be matched using propensity score calculated from baseline variables. For effectiveness outcomes, a descriptive analysis will be performed for all variables. For persistence assessments Kaplan-Meier assessments will be completed. For safety outcomes, all the safety data will be summarized through appropriate data tabulations, descriptive statistics, and graphical presentation.

- **Milestones**

Start of data collection	31 October 2017
End of data collection	30 June 2022
Registration in the EU PASS register	31 Oct 2017
Final study report	30 May 2023