NON-INTERVENTIONAL PROTOCOL ABSTRACT NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: Early access tofacitinib use in Australia: an observational study

Name, degree(s)	Title	Affiliation	Address
Dr/Prof Jakob Begun, Dr/Prof Jakob Begun, MD PhD	IBD Group Leader, Mater Research Ltd, Clinical Lead in IBD at Mater Hospital	Mater Research and Hospital	Department of Gastroenterology, Salmon Building, Level 4, Raymond Terrace, South Brisbane, Qld 4101

Rationale and background:

Tofacitinib was approved for the treatment of UC by the Australian Regulatory Agency (TGA) in February 2019. It does not yet have public reimbursement by the Pharmaceutical benefits scheme (PBS), but has been supplied on a case by case basis by Pfizer for physicians requesting it for their patients. Currently, there are more than 300 UC patients who have been treated with tofacitinib since TGA approval. The vast majority of them have failed previous biologic therapy. There has been very limited data presented on the response of patients to tofacitinib after previously failing anti-TNF and anti-integrin therapies. This data may be particularly germane to the Australian prescribing landscape where the positioning of tofacitinib in UC patients is not yet established.

The study proposes to examine the disease characteristics and outcomes in UC patients granted access to tofacitinib in Australia using deidentified patient information.

Research question and objectives: Examine the disease characteristics and outcomes in ulcerative colitis patients granted access to tofacitinib in Australia using deidentified patient information.

The primary outcome for this study is clinical response at the end of induction (week 8-12) and week 16 (defined as a decrease in the partial Mayo score by 2 or a partial Mayo score <2). The secondary endpoints include clinical remission at week 8-12 and week 16 (partial Mayo score <2 with no individual sub score greater than 1) resolution of rectal bleeding, endoscopic healing in those who had endoscopy, need for extended induction (16 weeks), cessation of steroids in those on steroids at commencement of tofacitinib, steroid free clinical remission at the end of induction (week 8 or 12) and week 16, improvement in calprotectin for patients with baseline and follow-up results and other biomarkers compared to the baseline characteristics where available. Reasons for discontinuation and to describe the safety profile of tofacitinib during treatment period with respect to AEs, SAEs, discontinuation due to AEs, and adverse events of special interest i.e. Hospitalization, Infectious complications, serious infections, Opportunistic Infections; Incidence of Herpes Zoster and extent (one or multiple dermatomes, ocular, systemic

disease), MACE (Major Adverse Cardiovascular Event), DVT (Deep Vein Thrombosis)/PE (Pulmonary Embolism)/VTE (Venous Thromboembolism); Malignancy – type and grade.

Study design: This is a longitudinal, retrospective, multi-center observational study.

Population: Patients who were granted access to tofacitinib since TGA listing in February 2019 with the Pfizer inclusion criteria (early access before listing with PBS); Patients with an established diagnosis of Ulcerative Colitis; Greater than 18 years of age; at least 16 weeks of patient safety follow-up, and up to 52 weeks, regardless of tofacitinib treatment duration.

Variables: Data collection will encompass demographics (age, gender), Montreal classification (disease extent and worst severity), disease duration, disease activity at time of tofacitinib commencement, partial Mayo Score, previous therapies (5-ASA, thiopurine, anti- TNF, anti-integrin or anti-interleukins), recent endoscopic severity, current steroid use (dose), inflammatory markers where available (CRP, calprotectin, ESR), lipids (if measured), SAE/AE's during treatment (hospitalization, infectious complications, incidence of Zoster an extent (one dermatome, multiple dermatomes, ocular, systemic disease), MACE, DVT/PE, NMSC, malignancies.

Data Sources: All data for this study will be obtained from treating physicians based on parameters collected during routine clinical practice. Physicians across Australia who have requested tofacitinib from Pfizer for their patients prior to public listing will be approached to participate in the study. After agreeing, they will be provided with case report forms for data entry. De-identified data will be collected, and completeness verified, including patient gender; summary of the patient's clinical history; prior treatments; outcomes and potential AEs after the use of Xeljanz. Data will be collected using digital case report forms. The deidentified data will be collected from each doctor and will be processed for further analysis.

Study Size: Power calculation – assuming $\alpha = 0.01$ and 90% power, 160 participants would be required to observe a minimum clinical difference between the published response rates for clinical response between placebo and tofacitinib. Fewer patients would also be adequate for analysis involving 80% power.

Data Analysis: Descriptive statistics will be used, no hypothesis testing or comparison to be done.

Milestones:

Milestone	Planned date
Start of data collection	22 October 2021
End of data collection	08 July 2022
Registration in the EU PAS register	30 September 2021
Final study report	19 August 2022