NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: Malignancy and Cardiovascular Risk Assessment Using the Consortium of Rheumatology Researchers of North America Registry (Corrona) as an External Comparator for Tofacitinib-Exposed Patients within the Rheumatoid Arthritis BID Clinical Trial Program: A Comparative Post-Approval Safety Study

Date: 09 March 2021

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Keywords: rheumatoid arthritis, tofacitinib, safety, matched analysis

Rationale and background: As of May 2016, 6300 patients were treated with tofacitinib for RA BID in clinical trials. Due to the design of the Phase 3 (P3) and long-term extension (LTE) studies, there were limited patient numbers and patient-years of exposure for comparators. External data sources were used to provide background rates for qualitative comparison to the clinical program safety data. This study sought to supplement these assessments by performing a formal comparison of malignancy and cardiovascular (CV) safety from the tofacitinib clinical trial program with data from the RA Corrona registry.

Research question and objectives: The objective of this study was to estimate the incidence rates and corresponding hazard rate ratios of malignancy and cardiovascular endpoints comparing patients from the tofacitinib RA BID clinical program to patients initiating a biologic DMARD and never exposed to tofacitinib (unexposed) in the Corrona registry.

Study design: An external comparison cohort study was conducted. Exposed (patients exposed to tofacitinib as part of the RA BID clinical trial program) and unexposed (patients from Corrona prescribed biologic therapies other than tofacitinib and never exposed to tofacitinib) were compared. There were adjustments for key clinical and demographic characteristics that differed between cohorts or were potentially associated with exposures and outcomes.

Setting: Data from the tofacitinib RA BID program (data cutoff of May 10, 2016) included all patients who received at least 1 dose of tofacitinib in completed Phase 1, Phase 2, Phase 3 and the LTE RA studies (P123LTE). Comparator data were derived from the Corrona Registry, an independent disease-based registry with prospectively collected patient and physician clinical data at more than 200 U.S. sites.

Subjects and study size, including dropouts: The primary comparator cohort consisted of 6300 tofacitinib exposed patients and 13,091 tofacitinib unexposed (Corrona bDMARD) patients. Secondary analysis specific to endpoint, tofacitinib therapy dose and geographical location (US) were conducted.

Variables and data sources: Baseline demographic and clinical characteristics, treatment history, comorbidities were aligned between the study cohorts. Safety endpoints of interest included all malignancies (excluding NMSC), major adverse cardiovascular events (MACE), non-fatal myocardial infarction and non-fatal stroke. Patient data for tofacitinib were collected in the context of the RA BID clinical trial program. Data from the registry were collected by clinicians for participating Corrona patients via targeted event of interest forms.

Results: Patients with RA who initiated tofacitinib within the clinical trial setting had a higher incidence of malignancies (excluding NMSC) when compared with bDMARD initiators within the Corrona Registry. Rates of CV events, including MACE, were similar between the patient populations. When stratified by dose, similar trends were noted.

Discussion: These results provide evidence that the risks of MACE, nonfatal MI and nonfatal stroke are comparable in patients with RA who received tofacitinib in the clinical trial setting versus bDMARD initiators in a large US patient population participating in a non-interventional study. Patients receiving tofacitinib in the clinical trial setting had a higher rate of malignancies (excluding NMSC) than bDMARD initiators in a large US patient population participating in a non-interventional study. Overall, the results of this study are consistent with the known safety profile of tofacitinib.

Marketing Authorization Holder(s): Pfizer Limited

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Document Approval Record

Document Name:	CT24-WI-GL15-RF01 1.0 NI Study Report Abstract 09 March 2021
Document Title:	A3921204

Signed By:	Date(GMT)	Signing Capacity
Campbell, Ulka	31-Mar-2021 02:20:33	Final Approval
De Bernardi, Barbara	08-Apr-2021 17:33:55	EUQPPV Approval