NON-INTERVENTIONAL PROTOCOL ABSTRACT

Version: 1.0 12 May 2020.

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Rationale and background

In December 2019, a novel coronavirus (severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)) emerged from China. The World Health Organization (WHO) declared the SARS-CoV-2 outbreak and associated disease (Coronavirus disease 2019 (COVID-19)) a global pandemic in March 2020 (WHO, 2020).[5] Patients with chronic rheumatic and gastrointestinal disease are considered a high-risk group for SARS-CoV-2 infection, given their susceptibility to infection, largely related to use of immunosuppressant therapies (eg, Murdaca, 2019).[3] Emerging data are conflicting as to whether compounds used to treat autoimmune conditions modify the clinical course of late stage infection via interruption of the proinflammatory cytokine storm (Sarzi-Puttini, 2020).[4] It remains unknown whether persons with RA, PsA or UC treated with Pfizer therapies are more susceptible to, or protected from, COVID-19.

Research question and objectives

The research questions addressed by this study are:

What proportions of SARS-CoV-2 diagnosed patients have a diagnosis of RA, PsA, or UC (ie, indicated subcohorts) or not (ie, non-indicated subcohort) and what is risk of serious clinical manifestations and outcomes of interest in these subcohorts?

Within the indicated subcohorts of SARS-CoV-2 diagnosed patients, what is the proportion treated at baseline with the following systemic therapies: tofacitinib, JAK inhibitors, TNFi, non-TNFi, and csDMARD and what is risk of serious clinical manifestations and outcomes of interest within strata?

Primary objectives:

- Within subcohorts of SARS-CoV-2 diagnosed patients, determine the proportions of patients with a diagnosis of RA, PsA, and UC (indicated subcohorts) and patients without any of these conditions (non-indicated subcohort).
- For each indicated subcohort and non-indicated subcohort, describe baseline demographic characteristics, treatment history and comorbidities.
- Within each indicated subcohort and non-indicated subcohort, estimate proportion experiencing serious clinical manifestations and outcomes of interest.

- Within each indicated subcohort of SARS-CoV-2 diagnosed patients, determine the proportions of patients treated with the following systemic therapies (class) at baseline: tofacitinib, JAK inhibitors, TNFi, non-TNFi and csDMARD (as monotherapy and combination therapy, as applicable).

- Describe patient characteristics, treatment history and comorbidities within baseline treatment strata.

- Estimate risk of serious clinical manifestations and outcomes of interest within baseline treatment strata.

- Determine the proportions of patients that continue baseline treatment after SARS-CoV-2 diagnosis within indicated subcohorts.

Study design

This is a retrospective cohort study involving secondary analysis of Optum administrative databases in the US consisting of longitudinal health information about patients tested for or diagnosed with SARS-CoV-2 infection.

Population

Analyses will be conducted using data from Optum's "Electronic Health Record Data for COVID-19" database, which contains a subset of the Optum EHR data set. This subset includes longitudinal EHR information for patients within the Optum network who have been tested for or diagnosed with SARS-CoV-2. This dataset has been curated specifically to provide access to near real-time structured, longitudinal health data for patients diagnosed with or tested for SARS-CoV-2.

Variables

Exposures: The exposures of interest include, but are not limited to, therapies used to treat the indicated populations (ie, csDMARDs, bDMARDs, tsDMARDs).

Outcomes: The outcomes of interest include, but are not limited to, hospitalization, ventilation, organ failure and death.

Covariates: The covariates of interest include, but are not limited to, patient characteristics and comorbidities.

Data sources

The structured data within Optum COVID testing database will be used to identify populations, exposures, confounders and endpoints of interest.

Study size

Given the descriptive nature of most analyses, there is no minimum sample size. Sample size achieved will depend on the number of patients testing positive for SARS-CoV-2 and the indication-specific rate of infections and will increase over time with subsequent data cuts.

Data analysis

The index date for each patient is defined as the first date that the study inclusion criteria are satisfied. Baseline variables and the endpoints of interest will be summarized as appropriate for categorical and continuous variables; 95% CI will be provided to show precision of the estimate.

Milestones

Milestone	Planned Date
Registration in the EU PAS register	17 May 2020
Start of data collection	18 May 2020
End of data collection	31 July 2022
Final study report	30 June 2023

1. Chow N, Fleming-Dutra K, Gierke R, et al (CDC COVID-19 Response Team). Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 – United States, February 12-March 28, 2020. MMWR, 2020; 69(13): 382-386.

2. The COVID Tracking Project at The Atlantic. https://covidtracking.com/data/us-daily (accessed 22 April 2020).

3. Murdaca G, Negrini S, Pellecchio M, et al. Update upon the infection risk in patients receiving TNF alpha inhibitors. Expert Opin Drug Saf, 2019; 18(3): 219-229.

4. Sarzi-Puttini P, Giorgi V, Sirotti S, et al. COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? Clin Exp Rheumatol, 2020; 38: 337-342.

5. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19—11 March 2020. Geneva, Switzerland: World Health Organization; 2020. https://www.who.int/dg/speeches/ detail/who-director-general-s-opening-remarks-at-the-media-briefingon-covid-19---11-march-2020.

6. Haberman R, Axelrad J, Chen A, et al.., Covid-19 in Immune-Mediated Inflammatory Diseases- Case Series from New York. NEJM, 2020. DOI: 10.1056/NEJMc2009567.