OHDSI Network Study: 2025 Bridging Evidence Gaps

Comparative Risk of Infection in Rheumatic Disease Patients Initiating Immunosuppressive Therapy

Background

- Rheumatic/autoimmune diseases (including myositis, scleroderma, lupus, uveitis) are a group of conditions associated with high morbidity and mortality
- Majority of patients are treated with immune-suppressing medications
- Infectious complications are a major contributor to adverse outcomes, driven largely by the immunosuppressive therapies used for treatment

Gaps in Current Evidence/Guidelines

Major gaps remain in comparative safety across rheumatic disease medications, including a lack of head-to-head data

There is also insufficient evidence on optimal vaccination strategies and antimicrobial prophylaxis

Quantification of risk largely unknown; “rare”, “sometimes”

Study Design

- **Population:** Adults aged ≥18 years with prevalent rheumatic disease, including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), inflammatory myositis (IM), or non-infectious uveitis, identified using previously validated OHDSI phenotype algorithms
- **Comparators**: Two complementary analytic aims will be pursued:
  - Aim 1 (Monotherapy comparisons): New users of mycophenolate mofetil (MMF), rituximab (RTX), intravenous immunoglobulin (IVIG), or Janus kinase inhibitors (JAKi; tofacitinib, baricitinib)
  - Aim 2 (Combination therapy comparisons)**:** Prevalent users of a conventional immunosuppressant (MMF, methotrexate [MTX], or azathioprine [AZA]) who initiate a second immunosuppressive agent (e.g., RTX, IVIG, JAKi), compared across alternative add-on strategies
- **Outcomes:**
  - Varicella zoster virus infection (shingles)
  - Hospitalized infection (composite)
  - Progressive multifocal leukoencephalopathy (PML)
  - Pneumocystis jirovecii pneumonia (PJP)
- **Design:** New-user and new-user/active-comparator designs. Time-to-event analyses will be conducted using propensity score–adjusted Cox proportional hazards models, with large-scale propensity scores derived from all available covariates in the OMOP-CDM. Negative control outcomes, subgroup analyses (e.g., vaccination and prophylaxis status), and multiple sensitivity analyses will be performed to assess robustness and residual confounding.

Participating Sites (thus far)

- Johns Hopkins
- Jansen (Johnson & Johnson)
- Columbia University
- Stanford University
- University of Southern California
- Penn State University
- UT Southwestern

The ask of the OHDSI Community:

1. Feedback on protocol:
    - design
    - assumptions
    - concept sets
    - analysis plans

2. Feedback on code (Strategus):
    - Does it match protocol intent?
    - Can it be more efficient?

3. If interested, participate as a data partner!

If you're still listening and interested…

- Protocol and code published to Microsoft teams page, OHDSI Forums, and GitHub

- Teams meetings on January 26th 10 AM EST and January 28th 11 AM EST for those interested:

  - OHDSI Rheumatology Network Study Feedback - January 26th
  - OHDSI Rheumatology Network Study Feedback - January 28th

- Message me at cmecoli1@jhmi.edu with questions