The feasibility of utilising the OHDSI network to generate large-scale evidence of the safety of biologics

Nicole Pratt
University of South Australia
BACKGROUND

- Biologic medicines what are they?
  - immune-based therapies used to treat cancer, diabetes, multiple sclerosis, heart attack, asthma, inflammatory bowel disease and autoimmune disorders such as rheumatoid arthritis
BACKGROUND

What’s the issue?

- While clinically effective, the unique mechanisms of action of biologics can result in unpredictable and life threatening adverse events
- Expanding indications, off-label use, use of multiple biologics for multiple diseases, and sequential use of biologics further exacerbates the potential for adverse events
- Pre-market clinical trials of biologics are limited by small sample sizes & some serious safety concerns have only emerged as populations have become increasingly exposed to biologics in the post-market setting

A review* of 174 biologics approved for use in the United States and Europe almost one-quarter of products required some safety-related post-market regulatory announcement

In South Australia, of 56 patients dispensed ipilimumab for malignant melanoma\(^1\), eight were admitted to hospital for severe, steroid refractory colitis and two of these patients received a colectomy after another biologic, infliximab failed to resolve the colitis.

In practice the rate of colitis was 3 times higher than in clinical trials and the estimated cost to manage the adverse events in these patients was over $400,000.
Another day another story.....

- **Efalizumab**, for treatment of psoriasis, was **withdrawn** 6 years post approval after three cases of PML were detected\(^2\)

- PML has also been identified post-market with **natalizumab**\(^3\), for treatment of multiple sclerosis, which resulted in a temporary removal from the market

  - Risk of PML was shown to **increase with duration** of use of natalizumab and **modified** with prior use of immunosuppressants
These examples highlight the need for a rapid post-market surveillance system for biologics that not only identifies and quantifies harms, but identifies particular characteristics that make patients more vulnerable to harm
Start the clock!

February 2017 - Application

Chief Investigators
Nicole Pratt, Libby Roughhead, Michael Ward, Lisa Kalisch Ellett (Australia)

Associate Investigators
Martijn Schuemie
Marc Suchard
Edward Lai, Yea-Huei Yang
Ian Wong
Ju-Young Shin, Nam-Kyong Choi
Michal Abrahamowicz
"The results of this work will generate real world evidence for regulators, clinicians and patients to support clinical decision-making."

"This is a very significant and innovative project. It involves a multi-national alliance and will produce globally relevant results and predictive models to inform identify and quantify safety problems arising with biologics and improve the clinical care of patients."

"The project addresses calls to action by international agencies and will impact human health given the rise in the development and use of biologic treatments. This is internationally important work and is likely to produce high impact papers and change treatment guidelines for biologics."
“There are two key weaknesses - the first is that the actual number of people on each biological within these possibly accessed datasets is not provided, the second is that the adverse outcomes that can be examined within these datasets is not clear...Is there an estimate for the number or proportion of patients in the Data Research Networks who have used or are using biologic treatments?”
Start the clock!

July 6 2017 – OHDSI in Action

An SQL query was posted on the OHDSI forum on 6 July 2017

SELECT COUNT(*) AS prescription_count
FROM drug_era
WHERE drug_concept_id IN (735843, 909959, 912263, 936429, 937368, 1110942, 1151789, 1186087, 1312706, 1314273, 1315411, 1387104, 1397141, 19041065, 19047423, 19080458, 19080982, 19100985, 40161532, 40167582, 40171288, 40222444, 40238188, 40241969, 40244266, 42801287, 44507676, 45774639, 45775965, 45892628, 45892883);

Thanks Martijn!
Start the clock!

July 7 2017 – OHDSI in Action

Results

15 different databases
Over 7 million biologic drug eras

Let’ put this into context.....Median number of subjects included in pre-market trials is between 438 and 1708*

*Duijnhoven RG, et al. Number of Patients Studied Prior to Approval of New Medicines: A Database Analysis. Plos Medicine 10(3) 2013
What’s next?

Population utilisation

Treatment pathways

Population-level Estimation

Patient-level Prediction
Protocol Coming Soon........