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

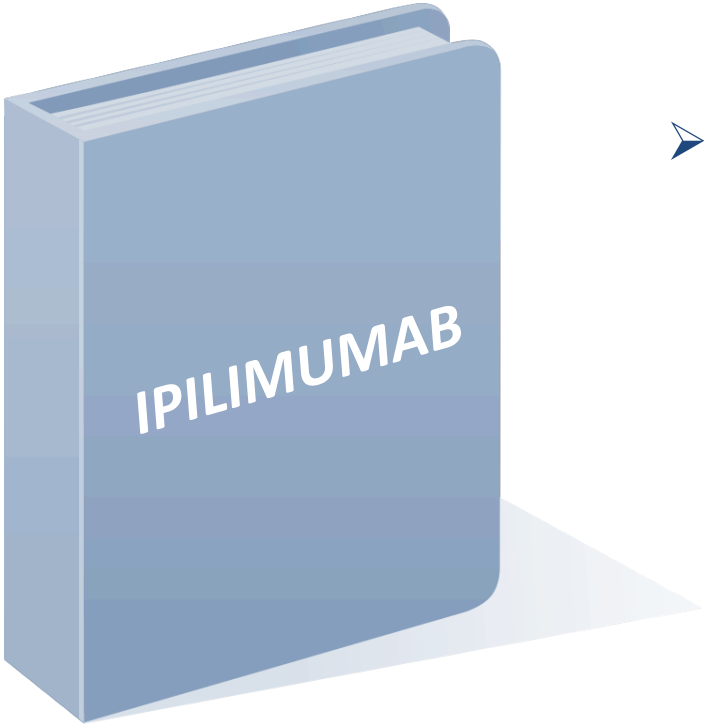
BACKGROUND

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*

*Giezen Tjet al. Safety-Related Regulatory Actions for Biologicals Approved in the United States and the European Union. JAMA. 2008; 300(16):1887-1896

Once upon a time…….

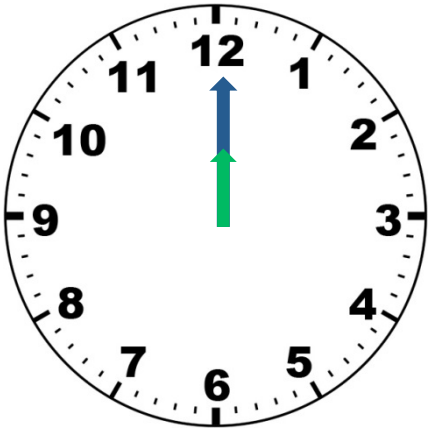


- In South Australia, of 56 patients dispensed **ipilimumab** for malignant melanoma[1], eight were admitted to hospital for severe, steroid refractory colitis and two of these patients received a colectomy after another biologic, **infliximab** failed to resolve the colitis.
  - In practice the rate 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- **Efalizumab**, for treatment of psoriasis, was **withdrawn** 6 years post approval after three cases of PML were detected[2]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**



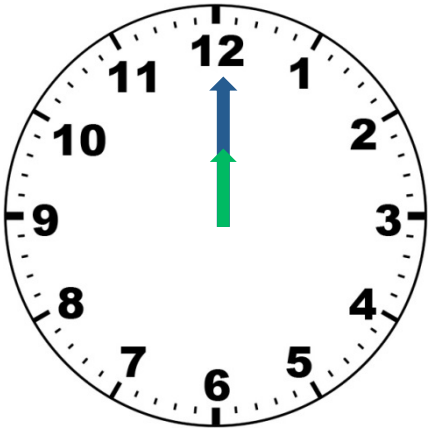
Start the clock!

February 2017 - Application

Australian Government
National Health and Medical Research Council

Chief Investigators
Nicole Pratt, Libby Roughead, 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



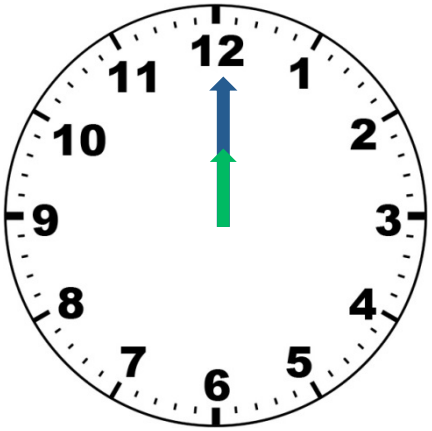
Start the clock!

July 2017 – Reviewers Comments

*"The results of this work will **generate real world evidence** for regulators, clinicians and patients to **support** clinical decision-making"*

"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."

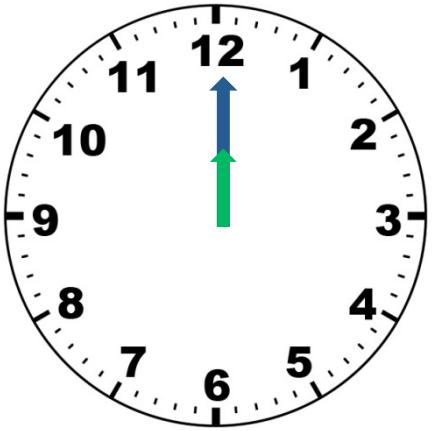
*"This is a very **significant** and **innovative** project. It involves a multi-national alliance and will produce **globally** relevant results and predictive models to inform identify and quantify safety problems arising with biologics and **improve** the clinical care of patients."*



Start the clock!

July 2017 – Reviewers Comments

"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?"



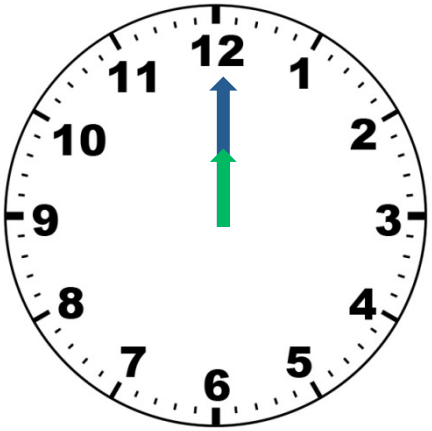
Start the clock!

July 6 2017 – OHDSI in Action

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

Thanks Martijn!

```
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);
```



Start the clock!

July 7 2017 – OHDSI in Action

Results

15 different databases

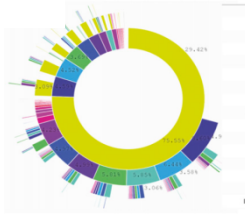
Over 7 million biologic drug eras

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?

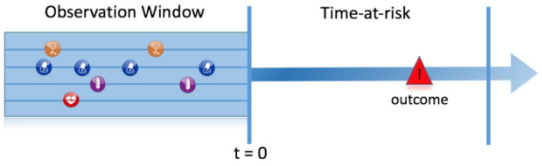
Population utilisation



Treatment pathways

KNOWLEDGEBASEWEB

Population-level Estimation



Patient-level Prediction

Protocol Coming Soon……

OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Who We Are | Standards | Software Tools | Methods | Research | Resources | Join the Journey | OHDSI Events | Past Events

2017 OHDSI Symposium | 2017 Tutorial Workshops | 2017 Collaborator Showcase | 2017 Symposium FAQs | Sponsors

Home › Network Research Studies

Network Research Studies

Study Name	Principal Investigator	Status	Participants
Comparison of combination treatment in hypertension	Seng Chan You, MD (Ajou University) Sungjae Jung, BE (Ajou University)	Protocol in development.	Martijn Schuemie (Janssen), Patrick Ryan (Janssen), Marc Suchard (UCLA)
Comparative effectiveness of alendronate and raloxifene in reducing the risk of hip fracture	Yeesuk Kim (Hanyang University), Marc Suchard (UCLA)	Analysis Ongoing. Paper in development.	Jon Duke, George Hripcsak, David Madigan, Christian Reich, Patrick Ryan, Martijn Schuemie
Large-scale modeling of patients with thyroid conditions	Antonija Burcul, Frank DeFalco (Janssen), Jill Hardin (Janssen)	Protocol in development.	Ivette Engel-Bicik, Maria Tulpan, Kent Holfort
Oral tetracycline-class Antibiotic Use for Acne Therapy	Lisa Schilling (UC Denver), Robert P. Dellavalle	In development. Seeking collaborators.	Stephanie Chapman, Renee Domozych, Jessica Mounessa, Jonathan Silverberg, David Barbieri, David Margolis
Learning Effective Clinical Treatment Pathways for Type-2 Diabetes from Observational Data	Rohit Vashisht (Stanford)	Study complete. Paper published in AMIA Annual Symposium Proceedings.	Martijn Schuemie (Janssen), Patrick Ryan (Janssen), Jamie Weaver (Janssen), Rae Wong Park (Ajou), Young Gun (Ajou), Nigam Shah (Stanford), Ken Jung (Stanford), Juan Banda (Stanford)
Large-Scale Population-Level Evidence Generation	Martijn Schuemie (Janssen), Patrick Ryan (Janssen)	Results presented at 2016 symposium. Seeking more collaborators.	Marc Suchard (UCLA), Peter Rijnbeek (Erasmus MC)