EUROPEAN FEDERATION OF STATISTICIANS IN THE PHARMACEUTICAL INDUSTRY
Representing Statistical Associations in Europe

Connecting the dots

How can statisticians drive end-to-end thinking in the development of new medicines?

HTA & Launch & Lifecycle Joint Session at PSI 2023 London
TUESDAY 13TH JUNE 2023 10:30-12:00

CASE STUDY 1

ATMP IN ONCOLOGY

BACKGROUND

- Personalized therapies such as ATMPs (Advanced Therapy Medicinal Products) are promising a long hoped-for leap in effectiveness, with simultaneously favorable tolerability profiles.
- Regulatory authorities such as the FDA and EMA increasingly see themselves approving these novel treatments in accelerated approval procedures based on single-arm studies.
- For the purpose of reimbursement, information on relevant comparators to contextualize the single-arm results are often only available in the form of aggregate data/summaries from publications.

HYPOTHETICAL EXAMPLE

Study design	Single arm trial
Population	Pretreated patients (mean 3 lines of prior therapies) with relapsed/refractory mantle cell lymphoma (r/r MCL)
Route of administration /dosing	One infusion after leukapheresis and bridging therapy if applicable, and a conditioning chemotherapy period
Mechanism of action (MoA)	Cell therapy (Advanced Therapy Medicinal Product/ATMP)
Context	• Personalized medicine with potential for cure for heavily pretreated and progressed patients • Marketing authorization is therefore often granted in accelerated approval procedures with single arm Phase II trials with limited or no comparative evidence available • Synthetic control arms are generated to show comparative effectiveness

SUGGESTED DISCUSSION POINTS

1. Challenges for Marketing Authorization?

- FDA and EMA are willing to accept single arm trials for breakthrough therapies, but on the other hand want to make sure that there is no harm for the patients
- Comparisons vs an external control arm (i.e. unanchored indirect comparisons) are a tool to address this challenge

What are your experiences as a statistician navigating regulatory discussions about external control arms?

2. Real-World data (RWD) or historical trial data for external control arms?

- Comparisons vs an external control arm have a high risk of bias and adjusting for confounders is of utmost importance
- RWD offers a possibility of using individual-level data that ma be very recent but less controlled; whereas historical clinical trial data might be older in time, without access to individual-level data, but collected in a more controlled way

As a statistician, what challenges do you face/foresee in finding the right data source for an external control arm?

3. Challenges in the HTA process?

- Comparisons vs an external control arm generally lead to conclusions with higher uncertainty
- HTA bodies, e.g. the G-BA in Germany, are willing to accept such evidence only if populations are similar, all confounders are adjusted for, and if effect sizes are large

What can statisticians do to lead discussions around quantification of bias? How can statisticians help to frame the certainty of results and drive discussions with HTA bodies?

4. Stakeholders?

- Due to the novel mechanism of action and the single-arm trial design, the whole process from trial design to launch in the countries is not standard.

With which stakeholders do you need to interact and how do they differ the lifecycle of a drug? How can statisticians help to strengthen understanding and collaboration between the different stakeholders?