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 2

LIPID-LOWERING THERAPY

BACKGROUND

- Cardiovascular disease (CVD) is a leading cause of death worldwide
- A key risk factor for CVD is increased lipid levels, particularly low-density lipoprotein (LDL-C)
- First-line treatment for lowering of LDL-C is statins, an oral therapy that works by slowing down liver LDL-C production. High-intensity statin can lower LDL-C by levels by 50-60%*
- Therapies with novel mode of actions are becoming available, including PCSK9 inhibitors which can reduce LDL-C by levels by 60%*, typically taken in combination with statins or as monotherapy

HYPOTHETICAL EXAMPLE

	ACCEPTABLE TARGET PRODUCT PROFILE	DESIRED TARGET PRODUCT PROFILE
Indication	Reduction of LDL-C	Prevention of CVD
Population	Patients with high LDL-C and a history of CVD (secondary prevention)	Patients with high LDL-C at high risk of CVD (primary prevention)
Route of administration /dosing	Oral capsule 40mg daily	
Mechanism of action (MoA)	Novel mechanism of action XYZ	
Co-administration	Monotherapy or combined w/statins	Monototherapy or combined w/statins and/or novel LDL-C lowering therapies
Context	• Launch into crowded/dynamic market; reduced timelines critical for competetiveness • Novel MoA suggests potential as combination therapy in particularly high-risk patients • Oral route of administration as key differentiator	

SUGGESTED DISCUSSION POINTS

1. BROAD VS NARROW LABEL?

- A broad regulatory label (→ broad pivotal trial population) may give apparent optionality down the line – but can leave more uncertainty to payers, who may only be able to reimburse a subpopulation
- Statistics, including subgroup analyses is often seen as a tool to resolve this challenge

What are your experiences navigating this discussion – at the design stage and post-hoc?

2. CLINICAL CONTEXT AT LAUNCH?

- In a crowded/dynamic market, it can be difficult to anticipate the clinical context at launch
- If e.g. competing novel LDL-C lowering therapies have become standard of care around launch, a pivotal trial would need to anticipate this to ensure relevance of the evidence from a payer/HTA perspective

How can statisticians help frame this discussion: 'save the pieces post-hoc' – or deal with it early on?

3. ENDPOINT ACCEPTABILITY?

- LDL-C is an established surrogate for cardiovascular outcomes in the epidemiological literature, and is also accepted by regulators
- However, surrogacy may be seen less favorably by payers/HTAs, who may challenge the relevance of historical surrogacy results for the case at hand.

What can statisticians do to lead discussions around evidence from surrogate outcomes?

4. VALUE OF AN ORAL?

- A therapy that differentiates mainly on route of administration (and not on efficacy/safety) may seem attractive from a patient/convenience perspective – but may not be readily attractive from a payer perspective

How can statisticians help shape the value story around an oral therapy?

* https://doi.org/10.1038/s41569-018-0107-8