Biomarker discovery across the dimensionality ladder

Joint Session: Biomarker + TEH SIG

Brief Introduction

GSK

Biomarker ESIG — 57 members from 33 companies/universities

European Special Interest Group Co-Leads:
Laura Schlieker (Staburo) and **Mathias Cardner** (AstraZeneca)

- The Biomarkers ESIG consists of three sub streams:
  - 🤖 Machine Learning (ML) & AI in Biomarkers, led by Nils Ternès and Karl Köchert
  - 🧬 Deciphering One Biomarker at a Time, led by Holly Tovey
  - 🌎 Strategic Advances for Precision Medicine, led by Achilleas Livieratos

- The sub stream devoted to ML/AI in Biomarkers researches and benchmarks methods:
  1. **Data-driven discovery:** Predictive/prognostic biomarkers and patient subgroups are typically inferred from **high-dimensional ($p > n$)** biomolecular data, possibly guided by prior knowledge
  2. **Collaborative efforts** on assessing **(causal) methods for predictive-biomarker discovery**
     - Kaggle-like initiative focused on hands-on data science involving biomarker data simulation, causal inference, and variable selection

Treatment effect heterogeneity SIG – 32 members from 14 companies!

European Special Interest Group Lead: **David Svensson** (AstraZeneca)

- Primary Focus: Assess the presence of treatment effect variability and explain it by **patient and disease characteristics** to identify **patient subgroups** that may benefit more or less from a given treatment.

- Types of subgroup analyses:
  1. **Pre-specified subgroups:** Patient subgroups may be pre-specified in advance based on existing clinical knowledge.
     - Ongoing collaboration on consistency assessment (e.g., using various Shrinkage approaches)
  2. **Data driven subgroup analysis:** Analysis methodology is pre-specified but relevant patient subgroups and characteristics driving their formation are discovered without a specific hypothesis.
     - Mostly consider baseline biomarkers and fewer potential markers (p<30).

Note a **difference between SIGs**: Identification of prognostic biomarkers may fall under the Biomarker SIG but not under the TEH SIG.

Theme: Biomarker discovery across the dimensionality ladder

From low-dimensional, hypothesis-driven markers to high-dimensional omics

Goal: Identify characteristics which drive treatment effect heterogeneity within a study population

- The session illustrates typical problems encountered in practice and highlights ongoing co-work activities in the two SIGs.
- Identification of predictive markers is an important step – towards tailoring treatment to patient subpopulations
- Many challenges are involved in this process including:
  - ✓ Early phase trials have limited sample size
  - ✓ Need for robust evidence to make regulatory decisions.
  - ✓ Varied considerations across dimensionality adds to the complexity.

Joint Session: Biomarkers SIG and Treatment Effect Heterogeneity SIG

Theme: Biomarker discovery across the dimensionality ladder

1. Presentation 1: A novel approach to assess the predictiveness of a continuous biomarker in early phases of drug development (**Marie-Karelle Riviere, Saryga**)

2. Presentation 2: Evaluating methods for biomarker cut-off detection: a comparative study in small and unbalanced samples (**Hugo Hadjur, Saryga**)

3. Presentation 3: Machine Learning in Precision Medicine: A Collaborative Approach (**Laura Schlieker, Staburo GmbH**)

4. Presentation 4: A Bayesian precision-medicine decision framework for pursuing biologically plausible predictive biomarkers in early clinical development (**Mathias Cardner, AstraZeneca**)

Chair: Ashwini Venkatasubramaniam, GSK

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