Servier Biometrics Intern Proposal

Early futility interim analysis using the Predictive Probability of Success based on primary and surrogate endpoints

Mentors: Ronan FOUGERAY and Loïck VIDOT**.**

Project background & overview:

The Predictive Probability of Success (PPoS) of a future clinical trial is a key quantitative tool for decision-making in drug development. It is generally derived from prior knowledge and evidence on the primary endpoint collected from previous clinical trials.

Because pharmaceutical industries are willing to speed up drug developments and to make early decisions regarding trials continuation/stop, we developed an innovative clinical trial design that includes an early futility interim analysis based on the PPoS. As only few information on the primary endpoint of the trial (OS) will be observed at the early futility interim analysis, PPoS calculation will also be based on a surrogate endpoint (PFS).

In this setting, an informative prior, called “surrogate prior”, is derived from (1) the information on the surrogate endpoint observed at the early futility interim analysis and (2) the joint distribution of the surrogate and primary endpoints, estimated using a meta-analytic approach on past clinical trials. Then, the few information on the primary endpoint observed at the early futility interim analysis is combined with the surrogate prior to generate the PPoS.

The objectives of this internship are to explore, implement and compare different approaches to deal with (1) potential prior data conflict (such as testing approach or mixture prior approach) between the surrogate prior and the observed primary endpoint data and (2) heterogeneity between past clinical trials used in the meta-analysis as well as primary and surrogate endpoints correlation.

In this scope, the trainee will:

- Perform a literature review to identify relevant approaches
- Develop programs extensions to implement selected approaches (R)
- Evaluate, compare & make recommendations about selected approaches considering various clinical trial settings using simulations on a real case oncology study

References:

G. Saint-Hilary et al: Predictive probability of success using surrogate endpoints

MJ. Daniels et al: Meta-analysis for the evaluation of potential surrogate markers

DJ. Spiegelhalter et al: Monitoring clinical trials: condition power or predictive power?

Training / Skills:

- Student in last year of engineering school in statistics or applied mathematics (ENSAI, INSA) or in Master 2 of Biostatistics or equivalent.
- Programming skills particularly with R language
- Communication skills (in writing and orally) in English
- Interest in life sciences is a plus

To apply:

Please contact Ronan FOUGERAY (ronan.fougeray@servier.com) and Loïck VIDOT (loick.vidot@servier.com).