Biomarker guided adaptive design with an intermediate endpoint in a seamless phase2/3 design in oncology drug development – Emmanuel Ogundimu (Durham University) & Adetayo Kasim (UCB Biopharma, UK)

Development of targeted therapies is accelerating in response to widespread identification of hypothesised biomarkers. A particular interest are candidate predictive markers believed to be related to the efficacy of an experimental treatment under study. This personalised medicine approach is a growing area of research which aims to tailor the treatment given to a patient according to one or more personal characteristics. These characteristics can be demographic such as age or gender, or biological such as a genetic or other biomarker.

Antoniou *et al.* (2016) provides a methodological review of the different biomarker-guided adaptive trial designs in Phase II and Phase III trials. The existing methods includes adaptive signature design, outcome-based adaptive randomisation design, adaptive threshold sample-enrichment design, adaptive patient enrichment design and multi-arm multi-stage (MAMS) design.

In this project we will evaluate the operating characteristics of adaptive signature design with an intermediate endpoint where a surrogate marker is used at interim analysis and primary endpoint is used at the end of the trial. It is also of interest to compare adaptive signature design and MAMS using simulation studies to investigate the impact of differential prevalence of a biomarker in the disease population

This project will require good knowledge of survival analysis and Bayesian methods. The project can be undertaking as an individual project with a limited scope, but preference will be for a group of students to work on the different parts of the project.

Reference

Antoniou M, Jorgensen AL, KolamunnageDona R (2016) Biomarker-Guided Adaptive Trial Designs in Phase II and Phase III: A Methodological Review. PLoS ONE 11(2): e0149803. doi:10.1371/journal.pone.0149803