Evaluation of a Bayesian Meta-model of tumour kinetics and survival

Tumour Growth Inhibitor-Overall Survival (TGI-OS) joint models are used to precisely characterize the association between tumour kinetics during treatment and risk of death in cancer patients[1]. Previous results suggest a good ability of joint modelling to predict outcome of a new trial by combining information of i) historical data in a similar population[2] (e.g. phase 2 trial to predict phase 3), and ii) early tumour follow-up from the ongoing trial[3]. Additional work needs to be done to assess its ability to predict the outcome of a new trial in different populations (e.g. new combination of treatment, primary tumour location or different disease severity).

This first requires quantifying the impact of different sources of between-studies variability in tumour growth, treatment effect and association with risk of death. Recently, our team has worked on developing a Bayesian TGI-OS meta-model, incorporating three levels of variability, namely i) lesion[4] ii) patient[1] and iii) study levels[5]. This hierarchical model structure combined with nonlinear description of tumour kinetics induces challenging inference that needs to be empirically validated.

In this internship, you will conduct a simulation study to validate the ability of HMC-NUTS algorithm (Stan software) to accurately estimate the various parameters of the Bayesian TGI-OS meta-model, under different scenarios.

Basic Qualifications & Skills:

- Master of Sciences (or equivalent) in data sciences, statistics/biostatistics or a related field
- Programming skills in R (preferred), Python or similar languages
- Good written and oral communication skills

Preferred Skills:

- Experience of hierarchical models and Bayesian paradigm
- Experience of Bayesian inference software (Stan or similar languages)

Work environment:

You will join team MOCLID (MOCLID | IAME - UMR 1137 IAME INSERM) based in the school of medicine of Bichat hospital (Paris 75018).

Supervision: Assil Merlaud, Dr Marion Kerioui, Dr Julie Bertrand (MOCLID | IAME)

Contact: marion.kerioui@mrc-bsu.cam.ac.uk; julie.bertrand@inserm.fr

References:

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2. Pitoy, A. *et al.* Isatuximab–dexamethasone–pomalidomide combination effects on serum M protein and PFS in myeloma: Development of a joint model using phase I/ II data. *CPT Pharmacomet. Syst. Pharmacol.* **13**, 2087–2101 (2024).
3. Kerioui, M. *et al.* Assessing the impact of organ-specific lesion dynamics on survival in patients with recurrent urothelial carcinoma treated with atezolizumab or chemotherapy. *ESMO Open* **7**, 100346 (2022).
4. Kerioui, M. *et al.* Nonlinear Multilevel Joint Model for Individual Lesion Kinetics and Survival to Characterize Intra-Individual Heterogeneity in Patients with Advanced Cancer. *Biometrics* **79**, 3752–3763 (2023).
5. Sudell, M., Kolamunnage-Dona, R., Gueyffier, F. & Tudur Smith, C. Investigation of one-stage meta-analysis methods for joint longitudinal and time-to-event data through simulation and real data application. *Stat. Med.* **38**, 247–268 (2019).