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Evaluating Early-Stage Oncology Clinical Trials in the Era of Project Optimus: A scoping review

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Marie-Karelle Riviere is Director Statistical Methodologist at Saryga, a company dedicated to support innovation in statistics and decision-making in healthcare. Jointly with her colleagues, she assists pharmaceutical companies, biotechnology companies and hospitals on developing and using advanced statistical methodologies to optimize drug development plans and clinical trials. With an active collaboration with academia, Saryga also contributes to the research and the publication of novel approaches.
Before joining Saryga, Marie-Karelle was in the Statistical Methodology Group at Sanofi in France where she provided support on complex innovative methodologies across all therapeutic areas and all development phases, but more specifically in early phases oncology. Marie-Karelle holds a PhD in Biostatistics from Paris-Diderot University on adaptive dose-finding designs in oncology. During her post-doc in pharmacometrics, she worked on the estimation of the Fisher information matrix for non-linear mixed effect models.

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Anais Andrillon is Statistical Methodologist at Saryga, a company dedicated to support innovation in statistics and decision-making in healthcare. Jointly with her colleagues, she assists pharmaceutical companies, biotechnology companies on developing and using advanced statistical methodologies to optimize drug development plans and clinical trials. Anais holds a PhD in Biostatistics from Université Paris Cité on adaptive dose-finding designs in oncology.

Pavel Mozgunov
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Pavel is an MRC Investigator (Programme Leader Track) working on the development and implementation of adaptive designs in clinical trials. Pavel provides statistical support in a number of trials, both publicly and privately funded.

Emma Gerard
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Emma Gerard is a biostatistician working in clinical drug development. She holds a master degree in biostatistics from Ensai (France) and a PhD in early oncology dose escalation methods from Université Paris Cité (France). She is currently employed by Sanofi R&D in France to work on statistical innovation in clinical trials.

Moreno Ursino
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Moreno Ursino is a researcher in biostatistics, equivalent to an associate professor, with expertise in the innovative design and analysis of clinical trials. His work focuses mainly on early-phase clinical trials, specializing in adaptive designs and the application of Bayesian

inference to optimize decision-making. He actively collaborate with multidisciplinary teams to address complex challenges in clinical studies.

Single topic, multi-speaker session, Workshop or Single presentation submission

A single presentation/poster

Single presentation or poster submission

In 2021, the FDA initiated the Project Optimus to reform the dose optimization and dose selection paradigm in early phase oncology. The traditional reliance on MTD has been increasingly questioned, and the identification of a dose that optimizes the risk–benefit trade-off of the drug or provides desired therapeutic effect whilst minimizing toxicity has been further advocated. The project also encourages early and comprehensive exploration of multiple doses during clinical development, advocates for a more patient-centered approach incorporating individual's response, biomarkers, PK/PD or patient-reported outcomes (PROs) to inform dosage decisions.

We propose a scoping review of the existing literature on early-phase oncology designs in light of the Optimus project. The review was organized according to the PRISMA-ScR guidelines. 160 journals were retained for the scoping review from which 641 papers were extracted with PubMed and SCOPUS search and within the scope of the review. Papers were then classified by type (statistical designs for early phase oncology, calibration of the methods, theoretical results, comparison of approaches, review or tools for practical application) and a list of items of interest was recorded (type of toxicity, efficacy and activity endpoint, time-to-events endpoints, inclusion of PRO, PK/PD or preclinical data, etc.).

The review aims to objectively determine which key elements of the Optimus guidelines are incorporated in the existing early-phase trial designs. It also aims to address the following question: What progress has been achieved so far, and what improvements can be made in light of the directives from Project Optimus?