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The Optimus Journey: FDA-Approved Examples of Dose Optimization in FIH Oncology Trials

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Benoit Sansas
Please provide a brief biography for the Presenting author(s)
Benoît is a Biometry Manager at Laboratoires Pierre Fabre in France, where he leads a team of Data Managers and Statisticians working in interventional clinical trials but also Real World Evidence trials. With 15 years of experience in biostatistics, from first-in-human studies to regulatory submissions, Benoît is particularly passionate about innovating ways of working and utilizing open-source solutions to improve and accelerate drug development. Since his graduation from National Institute of Applied Science (INSA) of Toulouse, he started his career in Preclinical and Research departments in pharmaceutical companies, before moving to clinical activities in Biotech, Pharma, and CRO organizations.

David Jegou
Please provide a brief biography for the Presenting author(s)
David is an experienced biostatistician with more than 15 years of experience. Currently serving as an Expert in Process Statistics at Laboratoires Pierre Fabre, he has previously led the statistics for early-phase oncology drug development within the same organization. His expertise includes developing adaptive designs and optimizing dose-finding processes in accordance with regulatory guidelines.

Eléna Dupuy
Please provide a brief biography for the Presenting author(s)
Elena Dupuy is a dedicated biostatistician with four years of experience in the pharmaceutical industry, currently working at Pierre Fabre Laboratories. Specializing in oncology clinical studies, Elena has worked extensively in early-phase clinical trials, focusing on innovative designs and study conduct for dose escalations and expansions.

Guillaume Desachy
Please provide a brief biography for the Presenting author(s)
Guillaume Desachy is driven by helping bring the right medicine to the right patient by leveraging the power of biometrics.

As Head of Biometrics at Pierre Fabre, he leads a department of 15+ experts in Data management, Programming and Statistics, working collaboratively to drive the success of both Clinical Trials and Real-World evidence studies. The Biometrics Department supports all drugs developed and commercialized by Pierre Fabre.

 Since his graduation from the French National School of Statistics (ENSAI) in 2011, he has had the privilege of working across all stages of drug development (from pre-clinical research to launch) across diverse landscapes, including academia (UCSF - U.S.), biotech ventures (Enterome - France) and global pharmaceutical industry leaders (BMS, Servier, AstraZeneca & Pierre Fabre - France & Sweden).

In addition to his role at Pierre Fabre, Guillaume is actively involved in various activities:
 Scientific Advisor for TrueYouOmics
 Visiting lecturer in OMICs data analysis & precision medicine at ENSAI
 Board Member of the ENSAI alumni association and of the French Statistical Society Biopharmacy & Health Group
⚖ Mentor at Article 1, an NGO promoting equal opportunity
 Co-lead of the EFSPI/PSI Biomarkers Special Interest Group

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

A single presentation/poster

Single presentation or poster submission

The FDA's Optimus project marks a significant shift in the approach to conducting First In Human (FIH) trials in oncology. Recognizing that the assumption of a linear efficacy dose-response is not always applicable, particularly in the fields of immunotherapies and targeted therapies, the FDA aims to enhance the dose optimization and selection paradigm. The traditional selection of the Maximum Tolerated Dose (MTD) as the Optimal Dose is no longer automatic, as a lower dose may offer the same efficacy with a better safety profile. A range of doses can now be explored to maximize the benefit-risk ratio.

In addition to safety, factors such as pharmacokinetics, relevant pharmacodynamic markers, and anti-tumor activity should be considered to determine the appropriate dose range for subsequent optimization. Therefore, selecting the right patient population from the start of FIH trials in the dose escalation phase is crucial. More efficient designs than the traditional 3+3 design, such as model-based or model-assisted designs combined with back-filling cohorts, have been developed to improve the dose-selection strategy. Early randomization is also an example of a solution to better optimize and select doses.

Our team has gained valuable experience through several FIH Investigational New Drug (IND) submissions in 2024, incorporating FDA feedback and design adjustments. This experience has led to a better understanding of the FDA's new expectations and improved trial designs. The journey of these two submissions, which align with the Optimus project and incorporate FDA comments, will be presented along with key recommendations for an Optimus-compliant development plan.