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A review of innovative seamless phase I/II design in early drug development in Oncology.

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Laurence Collette, PhD, currently works as a Statistics Director in Oncology Biostatistics at GSK where she is the biostatistics lead for oncology oncology business development. Prior to joining GSK, Laurence was Head of Statistics at the European Organisation for Research and Treatment of Cancer. She has over 25 years of experience in oncology clinical trials, from early development of new assets to post-marketing studies and biomarker development.

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Adetayo currently works as a Statistics Director in Oncology Biostatistics at GSK. Prior to this, he was a Professor of Statistics at Durham University, UK, where he continues to hold the title of Honorary Professor. Additionally, he is a Visiting Professor at the School of Pharmacy, Newcastle University, UK.

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Yoko Franchetti is an Associate Director of Clinical Pharmacology Modeling and Simulation Oncology at GSK. She has 20 years of combined experience in the industry and academia, at Regeneron, FDA ORISE, Dana-Farber Cancer Institute (DFCI), Epidemiology Data Center, and Nippon Shinyaku Co. Ltd. At DFCI, she worked as an ECOG-ACRIN statistician. She has an interest in dose/exposure-response analysis and designing studies using quantitative medicine methodologies in drug development. Yoko earned her BSc in Pharmaceutical Sciences from Kyoto University, her PhD in Clinical Pharmacology from the School of Pharmacy, and another PhD in Biostatistics from the Graduate School of Public Health, the University of Pittsburgh. Yoko is a licensed pharmacist in Japan, a member of multiple professional societies including ASA, and an editorial board member of the Journal of Clinical Pharmacology.

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

A single presentation/poster

Single presentation or poster submission

Finding the right dose/schedule is the first condition for successful drug development. The quest for choosing the right dose and/or schedule involves all stages of early drug development, including pre-clinical and translational studies. Traditionally, the first in-human studies focus on evaluating safety. However, it has become increasingly important

to also investigate activity, particularly in molecular targeted agents, immunotherapy, T-cell engagers, where a higher dose may not augment activity.

Project Optimus underscored the paradigm shift in oncology dose optimization. Optimal biological dose, which maximizes efficacy without increasing toxicity, is the emerging objective in methodology research. However, most trials still use maximum tolerated dose-focused dose-escalation methods, despite that multiple innovative methods to combine both traditional phase I (Safety) and phase II (activity) objectives exist. Although there have been reviews and insightful discourse about these methods, there is limited discussion on why these innovative methods are rarely used in practice.

In this presentation, we will discuss reasons why some of the methods cannot be used in practice. For this, we will focus on a review of the key methods, the type of data required, when this data is likely to be available, and the implications of the methods for other endpoints. We will highlight the gap between developing an innovative method and the potential utility of the method in practice. We will also make a case for closer collaboration between drug developers and academics to ensure innovative methods are developed with a deeper understanding of their applicability in actual clinical trials.