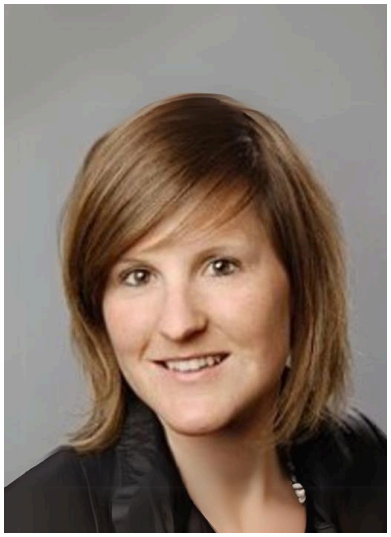
GLOBAL GATORS SYMPOSIUM

BILBAO SPAIN

Mirjam Trame

Bio



Mirjam Trame is a pharmacometrics consultant within Certara Drug Development Solutions and the US Lead for Pharmacometrics Division-II. Despite working on a variety of different modalities including complex biologics, she provides expert support in cell and gene therapy. Prior to joining Certara in early 2022, Mirjam worked in clinical development, clinical pharmacology, pharmacometrics, and systems pharmacology in industry and academia for > 20 years with a focus on complex biologics and cell and gene therapy for > 5 years.
She received her Ph.D. in Clinical Pharmacology and Pharmacometrics from the Westfälische-Wilhelms Universität in Münster, Germany, her Pharm.D. from the University of Florida, and her B.S. in Pharmaceutical Sciences from the Westfälische-Wilhelms Universität in Münster, Germany.

Abstract

Brief description: Combined pharmacometrics (PMX) and quantitative systems pharmacology (QSP) approaches have been more commonly applied in the early clinical development of bispecific antibodies in oncology in order to shed light into the dose response relationship. In this presentation, we will highlight how a joined PMX and QSP analysis of bispecific antibodies can guide step-up dosing in the early clinical development. The PMX analysis supported an early understanding of the dose and exposure relationship to the observed safety signals, increase in cytokine release syndrome (CRS) with increasing doses and exposures, and observed efficacy signals, decrease in time-to-progression (TTP) with increasing doses and exposures. The QSP model was developed to predict trimer formation in relationship to the efficacious dose levels as the observed decrease in TTP was hypothesized to be i) a result of overdosing the bispecific antibody leading to a favorable development of dimers over Target trimers or ii) factors unbalanced by dose group at higher dose levels. Both, the PMX and QSP model, were jointly used to predict the potential influence of patient factors influencing efficacy and safety signals. In addition, the joined PMX and QSP analysis was utilized to guide a step-up dosing regimen based on the triangulated information on trimer formation (QSP) and probability of CRS occurrence based on the PMX analysis.