NCS Non-Clinical Statistics Conference
Padua, IT / 23 – 25 September 2026

TITLE: Statistical Methodologies for Pragmatic AUC Estimation in Longitudinal Imaging Data

SPEAKER and COAUTHORS: Yuyue Liao[1], Martin Kohs[2], Lea A.I. Vaas[1]

[1] Bayer AG Pharma R&D, DSAI, Scientific Insight Solutions
[2] Bayer AG Pharma R&D, RED Oncology, Research Oncology

ABSTRACT:

Background: The Area Under the Curve (AUC) is a critical metric for summarizing longitudinal data in pharmaceutical research, particularly in areas such as radiopharmaceuticals and pharmacokinetics. This presentation discusses advanced methods for AUC calculation and deals with the complexities associated with longitudinal measurements under pre-clinical designs, including small sample size, sparse time points, and heterogeneous variabilities. These discussions are illustrated with PET-CT imaging example-data from Targeted Radiotherapies (TRT), representing precision radiopharmaceutical treatments.

Methodology: Individual subject data, following bolus, oral, and infusion patterns in pharmacokinetics, are simulated based on ranges, peaks, and measured time points derived from a set of real-world TRT data. Numerical integration methods for AUC calculation, including linear and log trapezoidal, cubic spline (Yeh and Kwan, 1978), and two hybrid approaches (Purves, 1992), are compared regarding their systematic bias. For the afterwards calculation of the variance of AUC for a group of subjects two approaches are compared: calculating (i) the AUC for each individual animal and subsequently determining the variance of these individual AUC values and (ii) the mean and covariance matrix of the endpoint at each time point before computing the AUC and its variance based on these aggregated statistics.

Results: The linear-up log-down and cubic-up log-down methods are practical approaches for AUC calculation, offering relatively smaller systemic bias under the challenge of sparse time points of TRT data. Calculating individual AUCs before determining variance is straightforward and requires no prior knowledge of the covariance structure. The alternative approach, being able to link AUC calculation to mixed models, is effective when no data transformation is needed or the covariance structure is known from prior knowledge, offering robustness against missing values. However, when these conditions are not met, only upper and lower bounds for AUC variance can be estimated.

Conclusion: In summary, this work proposes practical approaches for AUC estimation in longitudinal imaging data with small sample size and sparse time points. By addressing the inherent challenges of data analysis in pre-clinical settings, our findings underscore the need for robust statistical methods to enhance the clarity and reliability of AUC calculations.

Keywords: Area Under the Curve (AUC), Longitudinal Data Analysis, Statistical Methods, Numerical Integration, Targeted Radiotherapies (TRT), PET-CT Imaging

References:

1. Yeh, K.C., Kwan, K.C. A comparison of numerical integrating algorithms by trapezoidal, Lagrange, and spline approximation. *Journal of Pharmacokinetics and Biopharmaceutics* **6**, 79–98 (1978). https://doi.org/10.1007/BF01066064
2. Purves, R.D. Optimum numerical integration methods for estimation of area-under-the-curve (AUC) and area-under-the-moment-curve (AUMC). *Journal of Pharmacokinetics and Biopharmaceutics* **20**, 211–226 (1992). https://doi.org/10.1007/BF01062525
3. Jawień, W. Searching for an optimal AUC estimation method: a never-ending task?. *J Pharmacokinet Pharmacodyn* **41**, 655–673 (2014). https://doi.org/10.1007/s10928-014-9392-y