Operational Challenges of Phase I Oncology Studies

Opportunity

Table 1. Relative Standard Error and Bias of PK Parameters for a Tyrosine Kinase Inhibitor Based on Rich and Sparse sampling - Drug with Long Half-life, 1-Compartment Model

Table 2. Relative Standard Error and Bias of PK Parameters for a Small Molecule with Potent Multi-kinase Inhibitor Activity Based on Rich and Sparse sampling - Drug with Short Half-life, 2-Compartment Model

Table 3. Relative Standard Error and Bias of PK Parameters for an Oral Drug that Induces Apoptosis Based on Rich and Sparse sampling - Drug with Long Elimination Half-life, 2-Compartment Model

Reference:

Population PK

Parameters

Reference: 10 cohorts with Rich Sampling (n=6)

First Two Cohorts with Rich Sampling (n=16)

+ 2 cohorts with sparse sampling (n=16)

+ 4 cohorts with sparse sampling (n=49)

Relative Standard Error| Bias

Dose

Population

Parameters

Reference: 5 cohorts with Rich Sampling (n=17)

First Two Cohorts with Rich Sampling (n=30)

+ 2 cohorts with sparse sampling (n=22)

+ 4 cohorts with sparse sampling (n=49)

Relative Standard Error| Bias

CONCLUSION

The above modeling and simulations suggests that sparse sampling strategies may be developed to optimize PK analysis in Phase I oncology studies. The proposed sparse sampling strategies were shown to be robust for a wide variety of products, with different PK behaviors (e.g., 1- or 2-compartment model), different half-lives (i.e., short and long) and for different types of dosing (e.g., BID, QD).

The sparse sampling strategy may facilitate enrollment of cancer patients and accelerate completion of dose-escalation studies. The implementation of M&S in Phase I oncology studies may also be used to integrate PK/PD knowledge for decision making (Aarons et al. Eur J Pharm Sci. 2001. 13(2):115-22).