NONMEM Simulation Dataset

Article Title: Population Pharmacokinetics of Pegylated Liposomal CKD-602 (S-CKD602) in Patients With Advanced Malignancies

Analyte(s): CKD-602

Model: 1 CMT IV Infusion Non-linear Elimination

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# NONMEM Dataset Variables and Descriptions

| **Data Item ID** | **Data Item Description** | **Format** | **Sig Digit Display** | **Units** | **Data Item Notes** |
| --- | --- | --- | --- | --- | --- |
| ID | Patient Identification Number | (Numerical Integer) | 4 | N/A | * Each subject has a unique ID value * ID should be sequential starting from 1 to n subjects throughout the dataset |
| TIME | Numerical Time from First Dose | XX.XXX | 5 | hr | * Actual time * Recorded on each record |
| TAD | Time After Most Recent Dose | XX.XXX | 5 | hr | * Actual time * Recorded on each record * Resets back to 0 for each additional dose after the first dose |
| DOSE | Total IV Dosage Administered | XXXXXXX | 2 to 7 | mg | * This variable is identical to AMT, but should be propagated forward for each record from the most recent dosing record (for each treatment/PK Visit). |
| AMT | Total IV Dosage Amount Data Item | XXXXXXX | 2 to 7 | mg | * If a value is entered into the AMT variable, the DV variables for that record should be set to 0 * Values should be positive and only located on the “dosing” records * For observation records, set to 0 |
| DUR | Infusion Duration | X.XX | 1 to 3 | hr | * Total duration of infusion * For observation records, set to 0 |
| EVID | Event Identification Data Item | 0 = Value in DV  1 = Dosing Event | 1 | N/A | * If EVID = 1, DV must = 0. |
| MDV | Missing Dependent Variable Data Item | 0 = Value in DV  1 = Missing DV | 1 | N/A | * If there is an observation value defined in the DV data item, the MDV variable should be set to 0 * If there is NOT an observation in the DV data item, the MDV variable should be set to 1 |
| CMT | Compartment | X | 1 | N/A | * For dosing records, model compartment that dose was administered * For observation records, model compartment that observation was taken |
| BSA | Body Surface Area | X.XX | 3 | m2 | * Subject body surface area at time of initial dose * Continuous covariate * Simulated from a normal distribution with mean: 1.91 and SD: 0.3 |
| LT | Liver Tumor | 0 - Absent  1 - Present | 1 | N/A | * Indicates whether liver tumor is present in subject * Categorical covariate * Simulated two covariate levels, each with 0.5 probability |
| V | Central Compartment Volume | X.XXXX | 5 | L | * Empirical Bayesian Estimate of the individual’s central volume * Value should be positive and the same for all records for a particular individual |
| VMAX | Maximal Velocity for Nonlinear Elimination | XXX.XX | 5 | ug/h | * Empirical Bayesian Estimate of the individual’s maximal clearance rate * Value should be positive and the same for all records for a particular individual |
| KM | Michaelis-Menten constant | XXX | 3 | µg/L | * Empirical Bayesian Estimate of the individual’s reaction rate constant * Value should be positive and the same for all records for a particular individual |
| ETA1 | Between Subject Variability | X.XXX | 5 | N/A | * Measurement of BSV for V |
| ETA2 | Between Subject Variability | X.XXX | 5 | N/A | * Measurement of BSV for VMAX |
| VSS | Volume Distribution at Steady State | XX.XX | 3 or 4 | L | * Calculated as V for a 1 CMT model |
| IRES | Individual Residual | XXX.XX | 4 or 5 | ug/L | * Difference between that individual’s observation and the average observation of the population, including residual variability |
| IPRE | Individual Prediction | XXX.XX | 4 or 5 | ug/L | * If a value is entered into the IPRE variable, the AMT variable for that record should be set to 0 * Simulated plasma level for a patient including inter-individual variability |
| DV | Dependent Variable Data Items | XXX.XX | 4 or 5 | ug/L | * Simulated plasma level for a patient, including inter- and intra-individual variability * If a value is entered into the DV variable, the AMT variable for that record should be set to 0 * Each time point at which DV variables are measured should be entered as a new record |
| PRED | Population Prediction | XXX.XX | 4 or 5 | ug/L | * Simulated population plasma level |
| RES | Residual | XXX.XX | 4 or 5 | ug/L | * Difference between that individual’s observation and the population level observation |