

## Supplemental Tables

**Table S1. Demographics and actinomycin-D dosing information from all patients in the pooled analysis dataset**

<b>Demographics</b> <b>(mean, range)</b>	<b>Historical</b> <b>(n=33)</b>	<b>Pilot</b> <b>(n=3)</b>	<b>Dosing</b> <b>(mean, range)</b>	<b>Historical</b> <b>(n=33)</b>	<b>Pilot</b> <b>(n=3)</b>
Age (yr)	8.6 (1.6-20.3)	12 (6-16)	Dose (mg)	1.1 (0.5-2)	1.59 (0.96-2.5)
Weight (kg)	31.4 (9.5-95.8)	59.6 (21.8-92.4)	Dose (mg/kg)	0.043 (0.016-0.072)	0.03 (0.02-0.044)
Gender, n (%)			No. Obs., n (%)	no clearing	with clearing
Male	21 (64)	2 (67)	CVL	145 (88)	17 (49)
Female	12 (36)	1 (33)	PIV	19 (12)	18 (51)
Diagnosis, n (%)			Concentration (ng/mL)		
Wilms tumor	9	0	CVL	12.6 (1.34-99.2)	13.8 (1.46-66.7)
Ewing sarcoma	7	1 (33)	PIV	19.5 (0.218-113)	13.6 (0.11-90.5)
Soft tissue sarcoma	6	0			
Rhabdomyosarcoma	5	2 (67)			
Primitive neuroectodermal tumor	4	0			

CVL, central venous line; PIV, peripheral intravenous line.

**Table S2. Comparisons of catheter contamination models**

Model	Description/ Assumption	Contamination Parameters	Advantages	Limitations
Catheter Covariate	Catheter sampling method as a categorical covariate on PK parameters	$V1 = \theta_1 \cdot \left(\frac{WT}{70}\right) \cdot \theta_2^{CATH}$ $CL = \theta_3 \cdot \left(\frac{WT}{70}\right)^{0.75} \cdot \theta_4^{CATH}$	Parsimonious	Non-physiological, no estimation of contamination
Baseline Contamination	Assumes drug contamination from the sampling catheter as a baseline endogenous concentration and included in individual predictions	<p><i>Fixed contamination:</i>  <math>CTM = \theta_9</math>  <math>IPRED = F + CTM</math></p> <p><i>Proportional contamination:</i>  <math>CTM = (\theta_9 \cdot \exp(-Ke \cdot TIME)) \cdot IPRED</math>  <math>IPRED = F + CTM</math></p> <p><i>Saturable binding contamination:</i>  <math display="block">CTM = \frac{B_{max} \cdot OBS}{Kd + OBS}</math>  <math>IPRED = F \cdot (1 + CTM)</math></p>	<p>Fewer assumption regarding catheter binding phenomenon or geometry</p> <p>More accurate description of drug binding phenomenon</p>	<p>Extent of contamination is not dynamic</p> <p>Not accounting for mass balance</p> <p>Lacking in vitro binding data for parameter estimation</p>
Catheter Clearance	Includes catheter depot and bound compartment and blood-draw return cycle dependent rate constants	$F2 = \theta_1$ $F5 = 1 - F2$ $K12 = \theta_8$ $K15 = \theta_9$ $Krinse = \theta_{10}$ $Kno = \theta_{11}$ $K52 = Krinse \cdot CYCL + Kno$ $Fbound = \theta_{12}$	More robust in depicting catheter kinetics processes, allows simulation of varied cycles of the “pull-push” clearing method	Highly parameterized for limited dataset

Bmax, maximal binding capacity; CATH, catheter; CL, clearance; CTM, contamination factor; F2, fraction unbound from catheter depot to central compartment; F5, fraction bound from catheter depot to bound compartment; Fbound, fraction dissociated from catheter bound to central compartment, IPRED, individual predictions; K12, rate constant from catheter depot to central compartment, K15, rate constant from catheter depot to bound compartment; K52, overall dissociation rate constant from catheter bound to central compartment; Kd, dissociation constant; Ke, rate constant for change in contamination factor; Krinse, dissociation rate constant in the presence of blood-draw return cycle; Kno, spontaneous dissociation rate constant from bound to unbound state; V1, volume of central compartment; WT, body weight

