

**Experiment Number:** S0609  
**Route:** Gavage  
**Species/Strain:** Mouse/B6C3F1

**Toxicokinetics Data Summary**  
**Test Compound:** AZT + TMP/SMX (mixture) combination  
**CAS Number:** AZTTMPSMX

**Date Report Requested:** 02/01/2017  
**Time Report Requested:** 13:02:00  
**Lab:** Research Triangle Institute International

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<b>Male</b>								
<b>Treatment Groups (mg/kg)</b>								
	<b>25/250 *</b>	<b>25/250 °</b>	<b>25/250 ~</b>	<b>25/250 #</b>	<b>50/250 *</b>	<b>50/250 °</b>	<b>50/250 #</b>	<b>100/250 °</b>
<b>Plasma</b>								
$C_{max}$ (ug/mL)	0.561	0.586	0.104	11.7	0.564	0.885	25.5	0.546
$T_{max}$ (hour)	1.00	0.500	4.00	0.500	0.333	0.500	0.167	0.500
Lambdaz (hour <sup>-1</sup> )				0.744			1.01	
$t_{1/2}$ (hour)				0.930			0.685	
Cl (mL/min/kg)				28.6			28.4	
$V_{1(F)}$ (L/kg)				2.30			1.68	
MRT (hour)				0.947			0.957	
$AUC_{0-t}$ (ug*hr/mL)	1.01	1.21	0.0520		0.831	2.24		0.725

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**Male**

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**Treatment Groups (mg/kg)**

	<b>100/250 ~</b>	<b>100/250 *</b>	<b>100/250 #</b>	<b>100/500 *</b>	<b>100/500 #</b>	<b>100/500 °</b>	<b>100/500 ~</b>	<b>25/1000 #</b>	<b>25/1000 *</b>
	<b>Plasma</b>								
$C_{max}$ (ug/mL)	0.509	0.728	48.2	0.805	40.2	0.389	0.191	10.1	0.357
$T_{max}$ (hour)	0.333	0.0833	0.333	1.00	0.0833	0.333	0.333	0.167	12.0
$\text{Lambdaz}$ (hour <sup>-1</sup> )			0.312		0.354			0.240	
$t_{1/2}$ (hour)			2.21		1.95			2.86	
Cl (mL/min/kg)			26.0		23.5			18.2	
$V_{1(F)}$ (L/kg)			4.97		3.96			4.49	
MRT (hour)			1.15		2.31			3.91	
$AUC_{0-t}$ (ug*hr/mL)	0.407	1.07		3.53		1.09	0.557		1.62

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<b>Male</b>									
<b>Treatment Groups (mg/kg)</b>									
	<b>25/1000 °</b>	<b>50/1000 ~</b>	<b>50/1000 *</b>	<b>50/1000 °</b>	<b>50/1000 #</b>	<b>100/1000 *</b>	<b>100/1000 ~</b>	<b>100/1000 °</b>	<b>100/1000 #</b>
	<b>Plasma</b>								
$C_{max}$ (ug/mL)	1.01	0.932	0.311	2.03	23.9	1.65	0.477	1.02	43.4
$T_{max}$ (hour)	6.00	0.333	0.333	0.500	0.0833	2.00	2.00	1.00	0.167
Lambdaz (hour <sup>-1</sup> )					0.126				0.120
$t_{1/2}$ (hour)					5.42				5.89
Cl (mL/min/kg)					12.7				14.4
$V_{1(F)}$ (L/kg)					5.97				7.36
MRT (hour)					5.02				4.85
$AUC_{0-t}$ (ug*hr/mL)	6.91	2.72	0.0506	5.82		3.67	0.679	6.35	

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<b>Female</b>							
<b>Treatment Groups (mg/kg)</b>							
	<b>25/250 *</b>	<b>25/250 °</b>	<b>25/250 #</b>	<b>50/250 #</b>	<b>50/250 *</b>	<b>50/250 °</b>	<b>100/250 *</b>
	<b>Plasma</b>						
$C_{max}$ (ug/mL)	0.287	4.63	11.2	23.3	0.419	0.572	0.802
$T_{max}$ (hour)	0.500	0.167	0.167	0.167	0.500	0.500	0.333
Lambdaz (hour <sup>-1</sup> )			0.408	0.414			
$t_{1/2}$ (hour)			1.69	1.67			
Cl (mL/min/kg)			11.0	31.5			
$V_{1(F)}$ (L/kg)			1.62	4.55			
MRT (hour)			2.99	1.21			
$AUC_{0-t}$ (ug*hr/mL)	0.475	1.08			0.651	1.29	0.640

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**Female**

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**Treatment Groups (mg/kg)**

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	<b>100/250 ~</b>	<b>100/250 #</b>	<b>100/250 °</b>	<b>100/500 #</b>	<b>100/500 °</b>	<b>100/500 ~</b>	<b>100/500 *</b>	<b>25/1000 °</b>	<b>25/1000 ~</b>
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**Plasma**

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$C_{max}$ (ug/mL)	0.254	44.2	0.425	36.3	0.329	0.167	1.81	0.798	0.0920
$T_{max}$ (hour)	0.333	0.333	0.167	0.333	0.333	0.167	12.0	0.333	3.00
$\text{Lambdaz}$ (hour <sup>-1</sup> )		0.582		0.576					
$t_{1/2}$ (hour)		1.19		1.21					
Cl (mL/min/kg)		30.4		28.1					
$V_{1(F)}$ (L/kg)		3.12		2.94					
MRT (hour)		1.32		1.79					
$AUC_{0-t}$ (ug*hr/mL)	0.209		0.208		0.615	0.142	6.04	3.55	0.0460

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**CAS Number:** AZTTMPMSX

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	<b>Female</b>								
	<b>Treatment Groups (mg/kg)</b>								
	<b>25/1000 *</b>	<b>25/1000 #</b>	<b>50/1000 *</b>	<b>50/1000 ~</b>	<b>50/1000 #</b>	<b>50/1000 °</b>	<b>100/1000 *</b>	<b>100/1000 °</b>	<b>100/1000 ~</b>
	<b>Plasma</b>								
$C_{max}$ (ug/mL)	0.147	14.6	0.245	0.281	16.7	1.07	0.365	1.20	0.342
$T_{max}$ (hour)	4.00	0.333	0.333	6.00	0.0833	2.00	0.333	1.00	0.333
Lambdaz (hour <sup>-1</sup> )		0.264			0.282				
$t_{1/2}$ (hour)		2.63			2.48				
Cl (mL/min/kg)		19.5			15.6				
$V_{1(F)}$ (L/kg)		4.43			3.34				
MRT (hour)		2.37			3.33				
$AUC_{0-t}$ (ug*hr/mL)	0.268		0.110	1.18		2.92	1.59	5.67	0.0837

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**Female**

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**Treatment Groups (mg/kg)**

**100/1000 #**

**Plasma**

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$C_{max}$ (ug/mL)	40.5
$T_{max}$ (hour)	0.167
Lambdaz (hour <sup>-1</sup> )	0.138
$t_{1/2}$ (hour)	4.98
Cl (mL/min/kg)	17.4
$V_{1(F)}$ (L/kg)	7.50
MRT (hour)	4.23
$AUC_{0-t}$ (ug*hr/mL)	

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## LEGEND

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Data are displayed as mean values

### MODELING METHOD & BEST FIT MODEL

WinNonlin (Model 200 and 201, WinNonlin Ver. 1.5A, Scientific Consulting, Inc. now Pharsight Corporation, Apex, NC); Non compartmental analysis

### ANALYTE

- # 3'-Azido-3'-deoxythymidine
- \* 3'-Amino-3'-deoxythymidine
- ~ 3'-amino-3'-deoxythymidine glucuronide
- ° Beta-D-glucuronide

### DOSING

Mice were administered a single oral dose of 3'-Azido-3'-deoxythymidine (AZT) plus Trimethoprim-Sulfamethoxazole (TMP/SMX) twice daily (ca. 6 hours apart) for 7 days (14 doses).

### TK PARAMETERS

$C_{max}$  = Observed or Predicted Maximum plasma (or tissue) concentration

$T_{max}$  = Time at which  $C_{max}$  predicted or observed occurs

$\lambda_{z}$  = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA  $k_e$  or  $k_{elim}$

$t_{1/2}$  =  $\lambda_{z}$  half-life,  $t_{1/2}$ , the terminal elimination half-life based on non-compartmental analysis

Cl = Clearance, includes total clearance

$V_{1(F)}$  = Apparent volume of distribution for the central compartment includes  $V_{d(F)}$ ,  $V_{(F)}$  for oral groups, and  $V_{c(F)}$

MRT = Mean residence time

$AUC_{0-t}$  = Area under the plasma concentration versus time curve, AUC, from time  $t_i$  (initial) to  $t_f$  (final),  $AUC_{last}$

**\*\* END OF REPORT \*\***