

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: 01/30/2017
Time Report Requested: 10:49:19
Lab: Research Triangle Institute International

Male							
Treatment Groups (mg/kg)							
	25.250 *	25.250 °	25.250 #	50.250 ~	50.250 *	50.250 #	100.250 *
	Plasma						
C_{max} (ug/mL)	0.592	1.45	16.3	0.501	1.20	25.5	1.98
T_{max} (hour)	0.500	1.50	0.167	0.333	0.333	0.0833	2.00
Λ_z (hour ⁻¹)			0.300			0.0180	
$t_{1/2}$ (hour)			2.30			36.3	
Cl (mL/min/kg)			21.9			22.3	
$V_{1(F)}$ (L/kg)			4.35			70.2	
MRT (hour)			1.52			1.52	
AUC_{0-t} (ug*hr/mL)	0.659	1.83		0.0997	1.26		5.00

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	Treatment Groups (mg/kg)							
	100.250 ~	100.250 °	100.250 #	100.500 *	100.500 ~	100.500 °	100.500 #	25.1000 *
	Plasma							
C_{max} (ug/mL)	0.167	0.486	60.3	2.27	0.0820	0.163	42.3	0.692
T_{max} (hour)	0.0833	0.167	0.167	8.00	12.0	0.333	0.167	0.167
λ_z (hour ⁻¹)			0.0660				0.0600	
$t_{1/2}$ (hour)			10.3				11.8	
Cl (mL/min/kg)			24.2				24.0	
$V_{1(F)}$ (L/kg)			21.5				24.5	
MRT (hour)			2.18				2.08	
AUC_{0-t} (ug*hr/mL)	0.0197	0.480		12.6	0.164	0.0229		1.95

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	Treatment Groups (mg/kg)							
	25.1000[#]	50.1000[#]	50.1000[~]	50.1000^o	50.1000[*]	100.1000[#]	100.1000[*]	100.1000^o
	Plasma							
C_{max} (ug/mL)	9.29	17.8	0.201	0.911	0.387	35.6	1.02	1.50
T_{max} (hour)	0.0833	0.0833	0.333	0.500	0.500	0.0833	0.167	0.333
λ_z (hour ⁻¹)	1.30					0.0300		
$t_{1/2}$ (hour)	0.535					22.8		
Cl (mL/min/kg)	69.3					32.7		
$V_{1(F)}$ (L/kg)	3.21					64.5		
MRT (hour)	0.945	2.91				4.76		
AUC _{0-t} (ug*hr/mL)			0.185	2.85	0.536		0.832	1.63

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	Female							
	Treatment Groups (mg/kg)							
	25.250[#]	25.250^o	25.250[*]	25.250[~]	50.250[*]	50.250[~]	50.250[#]	100.250[#]
	Plasma							
C_{max} (ug/mL)	16.0	0.418	0.405	0.320	1.04	0.399	26.4	49.9
T_{max} (hour)	0.167	0.167	0.167	2.00	0.500	0.167	0.167	0.333
λ_z (hour ⁻¹)							0.294	0.0900
$t_{1/2}$ (hour)							2.38	7.68
Cl (mL/min/kg)							29.1	25.0
$V_{1(F)}$ (L/kg)							5.99	16.6
MRT (hour)	8.02						1.49	2.31
AUC_{0-t} (ug*hr/mL)		3.10	0.218	0.317	1.59	0.692		

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Female

Treatment Groups (mg/kg)

100.250 ° 100.250 * 100.500 * 100.500 # 25.1000 * 25.1000 #

Plasma

C_{max} (ug/mL)	0.269	0.626	5.37	38.5	0.225	7.73
T_{max} (hour)	0.500	0.333	12.0	0.167	0.167	0.0833
λ_z (hour ⁻¹)				0.0180		0.720
$t_{1/2}$ (hour)				35.9		0.966
Cl (mL/min/kg)				17.8		65.2
$V_{1(F)}$ (L/kg)				55.4		5.45
MRT (hour)				4.30		1.06
AUC_{0-t} (ug*hr/mL)	0.155	1.21	11.5		0.0647	

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	Treatment Groups (mg/kg)							
	50.1000 *	50.1000 °	50.1000 #	50.1000 ~	100.1000 ~	100.1000 *	100.1000 °	100.1000 #
	Plasma							
C_{max} (ug/mL)	0.104	0.807	16.1	0.278	0.413	0.839	1.01	25.7
T_{max} (hour)	1.00	0.500	0.167	0.500	0.0833	0.333	0.333	0.0833
Λ_{z} (hour ⁻¹)			0.0180					0.210
$t_{1/2}$ (hour)			36.4					3.30
Cl (mL/min/kg)			14.5					38.8
$V_{1(F)}$ (L/kg)			45.8					11.1
MRT (hour)			2.99					4.70
AUC_{0-t} (ug*hr/mL)	0.170	2.21		0.405	0.0703	0.623	0.728	

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LEGEND

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 given a single oral dose of AZT combined with Trimethoprim-Sulfamethoxazole (TMP/SMX) on Study Day 1

TK PARAMETERS

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

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

λ_{dz} = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA k_e or k_{elim}

$t_{1/2}$ = λ_{dz} 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 ****