

Experiment Number: S0553

Route: Gavage

Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary

Compound: 3'-Azido-3'-deoxythymidine/Rifampicin

Analyte: 3'-Amino-3'-deoxythymidine

CAS Number: AZTRIFAMPIN

Request Date: 7/11/2023

Request Time: 10:03:16

Lab: RTI

Male

Treatment Group (mg/kg)

100 AZT/100 RIF Gavage Plasma^{a,b}

Cmax_obs (ug/mL)	0.500
Tmax_obs (minute)	10
AUC_0-T (ug*min/mL)	47.3

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Request Time: 10:03:16

Lab: RTI

Female

Treatment Group (mg/kg)

100 AZT/100 RIF Gavage Plasma^{a,b}

Cmax_obs (ug/mL)	0.347
Tmax_obs (minute)	20
AUC_0-T (ug*min/mL)	56.4

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Male

Treatment Group (mg/kg)

100 AZT/100 RIF Gavage Plasma^{a,d}

Cmax_pred (ug/mL)	87.0
Tmax_pred (minute)	10
Beta Half-life (minute)	27.0
Cl ₁ _F (mL/min/kg)	32.6
MRT (minute)	38.1
AUC _{inf} _pred (ug*min/mL)	3069
F	0.86

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Female

Treatment Group (mg/kg)

100 AZT/100 RIF Gavage Plasma^{a,d}

Cmax_pred (ug/mL)	61.8
Tmax_pred (minute)	20
Beta Half-life (minute)	25.0
Cl ₁ _F (mL/min/kg)	35.5
MRT (minute)	39.3
AUC _{inf} _pred (ug*min/mL)	2816
F	0.66

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Route: Gavage

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Toxicokinetics Data Summary

Compound: 3'-Azido-3'-deoxythymidine/Rifampicin

Analyte: 3'-Azido-3'-deoxy-5'-beta-D-glucofuranosylthymidine

CAS Number: AZTRIFAMPIN

Request Date: 7/11/2023

Request Time: 10:03:16

Lab: RTI

Male

Treatment Group (mg/kg)

100 AZT/100 RIF Gavage Plasma^{a,c}

Cmax_obs (ug/mL)	1.14
Tmax_obs (minute)	20
AUC_0-T (ug*min/mL)	49.8

Experiment Number: S0553

Route: Gavage

Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary

Compound: 3'-Azido-3'-deoxythymidine/Rifampicin

Analyte: 3'-Azido-3'-deoxy-5'-beta-D-glucopyranurosylthymidine

CAS Number: AZTRIFAMPIN

Request Date: 7/11/2023

Request Time: 10:03:16

Lab: RTI

Female

Treatment Group (mg/kg)

100 AZT/100 RIF Gavage Plasma^{a,c}

Cmax_obs (ug/mL)	0.582
Tmax_obs (minute)	20
AUC_0-T (ug*min/mL)	21.3

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Toxicokinetics Data Summary

Request Date: 7/11/2023

Route: Gavage

Compound: 3'-Azido-3'-deoxythymidine/Rifampicin

Request Time: 10:03:16

Analyte: 3'-Amino-3'-deoxythymidine/3'-Azido-3'-deoxy-5'-beta-D-glucofuranosylthymidine/3'-Azido-3'-deoxythymidine/Rifampicin

Species/Strain: Mouse/B6C3F1

CAS Number: AZTRIFAMPIN

Lab: RTI

LEGEND

MODELING SOFTWARE

PCNONLIN software Version 4 .2,

MODELING METHOD & BEST FIT MODEL

^aPCNONLIN software Version 4 .2, SCI Software, Apex, NC, non-compartmental analysis

EXCEPTIONS

^bAMT t_{1/2}Beta were calculated from 15 to 150 minutes. For AUClast (AUC_{0-T}) the time the last plasma sample was obtained was 420 minutes.

^cGAZT t_{1/2}Beta were calculated from 15 to 60 minutes. For AUClast (AUC_{0-T}) the time the last plasma sample was obtained was 90 minutes.

^d20-180 minutes is the time interval over which t_{1/2}Beta was calculated. CI is apparent clearance.

ANALYTE

3'-Amino-3'-deoxythymidine

3'-Azido-3'-deoxythymidine/Rifampicin

3'-Azido-3'-deoxy-5'-beta-D-glucofuranosylthymidine

Experiment Number: S0553

Toxicokinetics Data Summary

Request Date: 7/11/2023

Route: Gavage

Compound: 3'-Azido-3'-deoxythymidine/Rifampicin

Request Time: 10:03:16

Analyte: 3'-Amino-3'-deoxythymidine/3'-Azido-3'-deoxy-5'-beta-D-glucopyranurosylthymidine/3'-Azido-3'-deoxythymidine/Rifampicin

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TK PARAMETERS

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

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

Beta Half-life = Half-life for the alpha phase

Cl_{1_F} = Apparent clearance of the central compartment, also Cl_{1_F} for gavage groups in non-compartmental model

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}

AUC_{inf_pred} = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

F = Bioavailability, absolute bioavailability

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Blood was analyzed for 3'-Azido-3'-deoxythymidine/Rifampicin (AZT), metabolite 3'-Azido-3'-deoxy-5'-beta-D-glucopyranurosylthymidine (GAZT), and metabolite 3'-Amino-3'-deoxythymidine (AMT) by HPLC with UV detection. Limit of detection (LOD) was estimated to be 0.042 ug/mL for AZT, 0.078 ug/mL for GAZT, and 0.015 ug/mL for AMT.

TK_GAVAGE PLASMA

100 mg/kg AZT/100 mg/kg RIF Male and Female

Animals weighed between approximately 20 and 30 g and were approximately 70-80 days of age at dosing. Animals received a single bolus dose either as an intravenous injection or oral gavage. Blood was collected at 13-14 timepoints from at least 3 mice per timepoint.