

Experiment Number: C88073C

Toxicokinetics Data Summary

Request Date: 7/11/2023

Route: Gavage

Compound: 2',3'-Dideoxyinosine (DDC)/ Analyte: 2',3'-Dideoxyinosine (DDC)

Request Time: 10:03:16

Species/Strain: Mouse/B6C3F1

CAS Number: 7481-89-2

Lab: RTI

Male

Treatment Group (mg/kg)

500 Gavage Plasma^a

1000 Gavage Plasma^a

Cmax_obs (ug/mL)	25.5	41.6
Tmax_obs (minute)	30	45
Beta Half-life (minute)	123.6	116.1
Cl (mL/min)	0.161	0.201
MRT (minute)	168.6	156.8
AUCinf_pred (ug/mL*min ⁻²)	3105	4975

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Female

Treatment Group (mg/kg)

500 Gavage Plasma^a

1000 Gavage Plasma^a

	500 Gavage Plasma ^a	1000 Gavage Plasma ^a
Cmax_obs (ug/mL)	41.0	36.9
Tmax_obs (minute)	45	30
Beta Half-life (minute)	184.9	117.4
Cl (mL/min)	0.115	0.179
MRT (minute)	138.3	176.0
AUCinf_pred (ug/mL*min ⁻²)	4330	5593

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CAS Number: 7481-89-2

Lab: RTI

Male

Treatment Group (mg/kg)

500 Gavage Plasma^a

1000 Gavage Plasma^a

Cmax_obs (ug/mL)	40.5	65.1
Tmax_obs (minute)	30	30
Beta Half-life (minute)	255.2	257.7
Cl (mL/min)	0.142	0.149
MRT (minute)	137.6	158.9
AUCinf_pred (ug/mL*min ⁻²)	3530	6729

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Lab: RTI

Female

Treatment Group (mg/kg)

500 Gavage Plasma^a

1000 Gavage Plasma^a

Cmax_obs (ug/mL)	53.2	83
Tmax_obs (minute)	15	45
Beta Half-life (minute)	107.1	107.7
Cl (mL/min)	0.100	0.098
MRT (minute)	97.5	138.9
AUCinf_pred (ug/mL*min ⁻²)	5009	10222

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LEGEND

MODELING SOFTWARE

Microsoft Excel/PCNONLIN

MODELING METHOD & BEST FIT MODEL

^aMicrosoft EXCEL (Version 5.0) and PCNONLIN (SCI Software, Lexington, KY), noncompartmental

ANALYTE

2',3'-Dideoxyinosine (DDC)

TK PARAMETERS

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

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

Beta Half-Life = Half-life for the beta phase

Cl = Clearance, includes total clearance

MRT = Mean Residence Time

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

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TK PARAMETERS PROTOCOL

ANALYSIS METHOD

The timepoints for blood collection are 5, 10, 15, 30, 45, 60, 90, 120, 240, 360, 480, 1080 minutes after the last dose; n=3. Each animal was sampled once. Blood was collected and plasma, separated. Plasma was analyzed by HPLC with UV detection (267 nm) and 2,6-diaminotoluene was used as an internal standard. C_{max} and T_{max} were determined by inspection of the plasma concentration vs. time curve. All beta half-lives were calculated from 360 to 1080 minutes except for that of the Swiss female mice at 500 mg/kg/day which was calculated from 120 to 480 minutes. Clearance was calculated using the total daily dose (500 or 1000 mg/kg). If the actual dose on the day of necropsy was equivalent to a morning dose only (250 or 500 mg/kg), then clearance values would be halved.

TK_GAVAGE PLASMA

500 mg/kg,1000 mg/kg Male and Female (Strain B6C3F1)

Male and female B6C3F1 mice were administered 500 or 1000 mg 2',3'-Dideoxycytidine (ddC)/kg bodyweight/day for 26 weeks (approximately 182 days) by gavage. Mice were dosed with ddC twice per day (20 mL/kg per dose) approximately 6 hours apart. The vehicle was 0.5% aqueous methylcellulose. On the last day of the study, animals were dosed (as usual) in morning and afternoon. On the day of necropsy, blood was collected from 3 animals approximately 18 hours after the afternoon dose of the previous day. Then, the remaining animals were dosed, and blood was collected at timed intervals.

500 mg/kg, 1000 mg/kg Male and Female (Strain CD-1)

Male and female NIH Swiss (CD-1) mice were administered 500 or 1000 mg 2',3'-Dideoxycytidine (ddC)/kg bodyweight/day for 26 weeks (approximately 182 days) by gavage. Mice were dosed with ddC twice per day (20 mL/kg per dose) approximately 6 hours apart. The vehicle was 0.5% aqueous methylcellulose. On the last day of the study, animals were dosed (as usual) in morning and afternoon. On the day of necropsy, blood was collected from 3 animals approximately 18 hours after the afternoon dose of the previous day. Then, the remaining animals were dosed, and blood was collected at timed intervals.