Experiment Number: K88073-1
Route: Gavage
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Compound: 2',3'-Dideoxyinosine/ **Analyte:** 2',3'-Dideoxyinosine
CAS Number: 7481-89-2

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: SO

Male

	Treatment Group (mg/kg)		
	84 Gavage Plasma[a]	**169 Gavage Plasma[a]**	**375 Gavage Plasma[a]**
Alpha Half-life (hour)	0.56	0.52	0.50
Beta Half-life (hour)	2380	9290	9.75
Cl (mL/hr*kg)	2610	3980	5580
AUC_0-T (ug*hr/mL)	32.2	42.5	67.2

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	Treatment Group (mg/kg)		
	750 Gavage Plasma[a]	**750 Gavage Plasma[a]**	**1500 Gavage Plasma[a]**
Alpha Half-life (hour)	0.60	0.46	0.73
Beta Half-life (hour)	7.90	9.96	2450
Cl (mL/hr*kg)	8930	6520	9430
AUC_0-T (ug*hr/mL)	84.0	115	159

LEGEND

MODELING SOFTWARE

NONLIN

MODELING METHOD & BEST FIT MODEL

[a]NONLIN, biphasic with no absorption phase

ANALYTE

2',3'-Dideoxyinosine (DDC)

TK PARAMETERS

Alpha Half-life = Half-life for the alpha phase
Beta Half-Life = Half-life for the beta phase
Cl = Clearance, includes total clearance
AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Plasma was harvested and frozen then extracted and analyzed by HPLC with UV detection (280 nm) using 5-chlorocytosine arabinoside as the internal standard. Plasma ddC values based upon the actual bleeding times were analyzed using a computer-based pharmacokinetics program (NONLIN) to calculate the AUC for each dose group. For the pharmacokinetic parameters the dose concentrations were converted to ug/kg. Plots show no absorption phase, elimination is biphasic with half-life of initial phase varying between 0.39 and 0.74 hours. Terminal beta phase was difficult to define as estimates for half-life beta were based upon 2 points/curve (for single dose) but the estimates for the two oral doses had 4 points. AUC was calculated for t=0 to 24 hours. This study will determine the relationship between the size of an oral gavage dose of ddC administered to B6C3F1 mice and the area under the plasma ddC 'concentration x time' curve to select dose levels for the potential 90 day subchronic study.

TK_GAVAGE PLASMA

84 mg/kg,169 mg/kg, 375 mg/kg, 750 mg/kg, 1500 mg/kg Male

Approximately 157-day old B6C3F1 male mice weighing between 36.9 and 46.0 grams were singly dosed with 84, 169, 375, 750, or 1500 mg/kg 2',3'-dideoxycytidine (ddC) by gavage. The vehicle was 0.5% (w/v) methylcellulose in deionized water and there were no vehicle control animals. Mice were weighed prior to dosing, and the oral doses were based upon these body weights. Blood samples were taken from different animals at 0.25, 1, 2, 4, 8, and 24 hours post dose (n=4) from the retro-orbital sinus in CO2 anesthetized mice.

750 mg/kg Male

Approximately 157-day old B6C3F1 male mice weighing between 36.9 and 46.0 grams were dosed twice with 750 mg/kg 2',3'-dideoxycytidine (ddC) by gavage approximately 6 hours apart. The vehicle was 0.5% (w/v) methylcellulose in deionized water and there were no vehicle control animals. Mice were weighed prior to dosing, and the oral doses were based upon these body weights. Blood samples were taken from different animals at 0.25, 1, 2, 4, 8, and 24 hours after the second dose (n=4) from the retro-orbital sinus in CO2 anesthetized mice.