

Experiment Number: K88074
Route: IV, Gavage
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Compound: 2',3'-Dideoxyinosine (DDI)/ **Analyte:** 2',3'-Dideoxyinosine (DDI)
CAS Number: 69655-05-06

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

Male

Treatment Group (mg/kg)

50 IV Plasma^a

250 IV Plasma^a

Alpha Half-life (minute)	1.86	5.81
Beta Half-life (minute)	36.8	36.7
Cl (mL/min*kg)	94.2	102.9
AUCinf_pred (ug*min/mL)	531	2430
F (percent)	100	100

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Treatment Group (mg/kg)

500 Gavage Plasma^b

1000 Gavage Plasma^b

2000 Gavage Plasma^b

Beta Half-life (minute)	30.0	31.8	66.4
k01 Half-life (minute)	2.37	6.78	0.50
Cl (mL/min*kg)	99.4	98.5	99.4
AUCinf_pred (ug*min/mL)	312	883	1710
F (percent)	6.2	8.7	8.5

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LEGEND

MODELING SOFTWARE
NONLIN

MODELING METHOD & BEST FIT MODEL

^aNONLIN, biphasic elimination

^bNONLIN, initial absorption phase followed by a monoexponential elimination phase.

ANALYTE

2',3'-Dideoxyinosine

TK PARAMETERS

Alpha Half-Life = Half-life for the alpha phase

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

k01 Half-life = Half-life of the absorption process to the central compartment

Cl = Clearance, includes total clearance

AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

F = Bioavailability, absolute bioavailability

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TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Plasma ddl data were analyzed with NONLIN. Bioavailability calculation $F = \text{AUC(PO)} / [\text{AUC(IV)} * M]$ where F= bioavailability, M = a normalizing factor = oral dose/IV dose. M is used to adjust for the difference in the size of doses administered. Bioavailability was approx. 6-9% or orally administered dose. Clearance iv = Dose (ug/kg)/AUC (ug-min/mL). Clearance oral = $[F * \text{Dose (ug/kg)}] / \text{AUC (ug-min/mL)}$ where F = bioavailability.

TK_INTRA VENOUS PLASMA

50 mg/kg, 250 mg/kg Male

Male B6C3F1 mice were singly dosed with 2',3'-dideoxyinosine (ddi) intravenously (50 or 250 mg/kg in deionized water) or by oral gavage (500, 1000, or 2000 mg/kg in aqueous 0.5% methylcellulose). Animals were weighed the day before dosing to determine dose volumes. At dosing, the average age was 56 days and the body weights ranged from 24.9 to 30.8 g. Animals were fed NIH-07 pelleted rodent feed and given tap water ad libitum. Blood samples were taken at 9 timepoints post dose (2, 5, 10, 15, 30, 45, 60, 90 and 120 minutes; n=3. Plasma was harvested for ddl concentration analysis using HPLC with UV detector (260 nm).

TK_GAVAGE PLASMA

500 mg/kg, 1000 mg/kg, 2000 mg/kg Male

Male B6C3F1 mice were singly dosed with 2',3'-dideoxyinosine (ddi) intravenously (50 or 250 mg/kg in deionized water) or by oral gavage (500, 1000, or 2000 mg/kg in aqueous 0.5% methylcellulose). Animals were weighed the day before dosing to determine dose volumes. At dosing, the average age was 56 days and the body weights ranged from 24.9 to 30.8 g. Animals were fed NIH-07 pelleted rodent feed and given tap water ad libitum. Blood samples were taken at 9 timepoints post dose (2, 5, 10, 15, 30, 45, 60, 90 and 120 minutes; n=3. Plasma was harvested for ddl concentration analysis using HPLC with UV detector (260 nm).