

**A**

PK parameters in mice after the intravenous administration of R-DXd.

Analyte	Dose (mg/kg)	AUC <sub>0-21d</sub> (day·µg/mL)	T <sub>1/2</sub> (h)	CL (mL/day/kg)	V <sub>ss</sub> (mL/kg)
R-DXd	0.25	5.76 ± 0.38	1.26 ± 0.20	44.1 ± 2.7	55.6 ± 6.4
	0.5	10.3 ± 2.0	1.21 ± 0.19	50.7 ± 11.1	56.7 ± 7.8
	1	30.9 ± 16.0	1.33 ± 0.67	43.1 ± 30.6	60.6 ± 3.2
	2	73.4 ± 36.4	1.30 ± 0.45	33.2 ± 18.4	59.3 ± 1.4
	4	173 ± 64	1.85 ± 0.40	25.0 ± 8.0	68.8 ± 7.3
	8	249 ± 29	2.55 ± 1.00	32.3 ± 3.8	84.6 ± 12.1

PK parameters were calculated based on the concentrations determined in plasma, which were collected 1, 6, 24, 72, 168, 336, and 504 h after the intravenous administration of R-DXd (0.25, 0.5, 1, 2, 4, and 8 mg/kg) using non-compartmental analysis. Each value represents the mean and SD (*N*=3).

AUC<sub>0-21d</sub>: area under the plasma concentration-time curve up to 21 days, T<sub>1/2</sub>: terminal elimination half-life, CL: total body clearance, V<sub>ss</sub>: volume of distribution in a steady state.

**B**

PK parameters in monkeys after the intravenous administration of R-DXd.

Analytes	Dose (mg/kg)	AUC <sub>0-28d</sub> (day·µg/mL)	T <sub>1/2</sub> (h)	CL (mL/day/kg)	V <sub>ss</sub> (mL/kg)
R-DXd	0.3	19.5 ± 3.7	2.61 ± 0.66	15.8 ± 3.5	47.7 ± 4.8
	1	110 ± 34	4.19 ± 1.26	9.71 ± 3.74	50.3 ± 4.2
	3	334 ± 28	6.32 ± 1.25	8.62 ± 0.88	69.1 ± 13.3
	10	874 ± 188	7.56 ± 0.78	11.2 ± 2.3	84.9 ± 8.4
Total Ab	0.3	17.5 ± 2.6	2.19 ± 0.37	NA	NA
	1	98.3 ± 30.1	4.05 ± 1.16	NA	NA
	3	309 ± 30	6.10 ± 1.12	NA	NA
	10	841 ± 199	7.93 ± 0.98	NA	NA

PK parameters were calculated based on the concentrations determined in plasma, which were collected 0.083, 1, 7, 24, 72, 168, 336, 504, and 672 h after the intravenous administration of R-DXd (0.3, 1, 3, and 10 mg/kg) using non-compartmental analysis. Each value represents the mean and SD (*N*=3).

AUC<sub>0-28d</sub>: area under the plasma concentration-time curve up to 28 days, T<sub>1/2</sub>: terminal elimination half-life, CL: total body clearance, V<sub>ss</sub>: volume of distribution in a steady state, NA: not applicable.