Characterization of Intravenous & Oral Pharmacokinetics : NCA method

Ramesh Jayaraman, DoseQuantics Consulting

The intravenous and oral PK of DQ2 was evaluated in mice (table 1). Graphical analysis was done (figure 1) and the Non-compartmental (NCA) PK parameters were estimated (table 2).

Table 1: Plasma mean concentration-time data of DQ2 in mice

time (h)	Plasma conc (µg/ml)	
	IV PK (10 mg/kg)	POPK (10 mg/kg)
0.030	24.23	NE
0.5	16.7	4
1	11.92	4.68
2	10.41	5.73
4	9.14	6
8	5.77	4.2
17	3.82	2.08
24	2.17	1.31
32	1.12	0.64

Figure 1: IV-PO PK curves of DQ2 in mice : log-linear plot

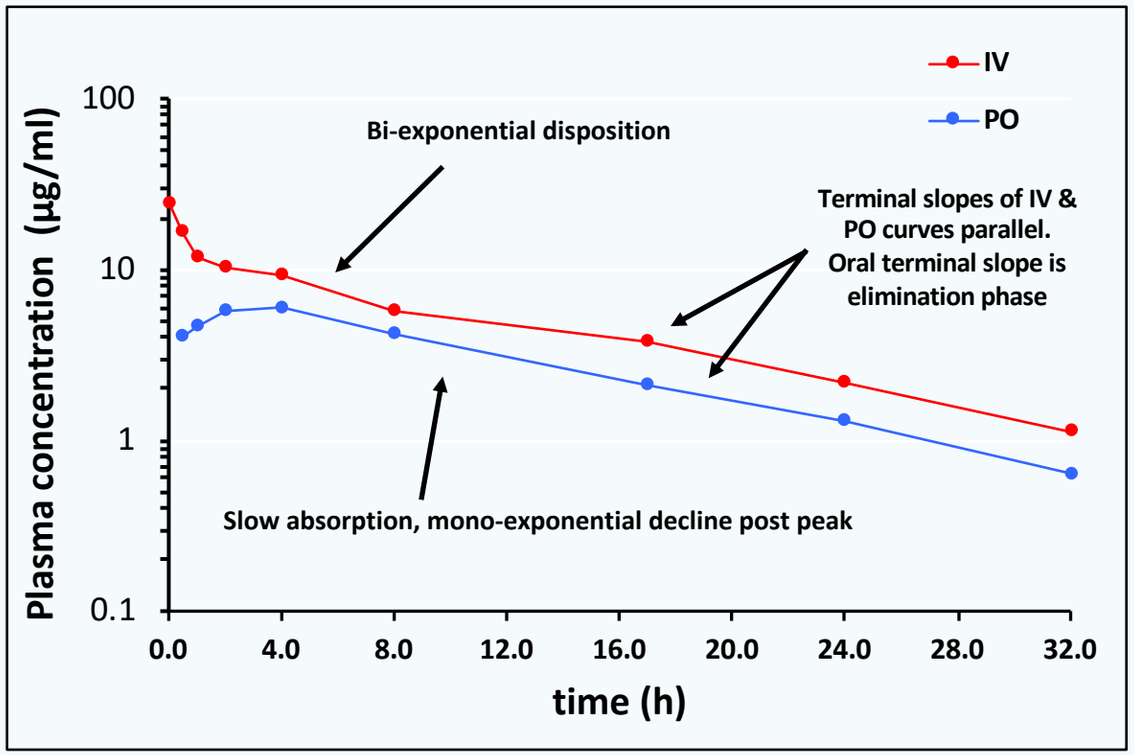

Table 2: NCA PK parameters of DQ2 in mice

IV PK

Parameter	Estimate	Remark
Dose (mg/kg)	10	
K_e (h^{-1})	0.071	
$t_{1/2}$ (h)	9.71	Long half-life. Time to steady state ~ 40h
AUC_{0-t} (µg.h/ml)	153	
$AUC_{0-\infty}$ (µg.h/ml)	170	To be compared with potency
$AUC_{extrapol}$ (%)	9.8	Extrapolated Area < 20%
Cl (ml/h/kg)	59	Low Clearance (1 % of Mouse Liver Blood flow (5.4 l/h/kg*))
V_{ss} (ml/kg)	799	Moderate Volume of distribution (~ Mouse Total Body water = 0.725 l/kg*)

Oral PK

Parameter	Estimate	Remark
Dose (mg/kg)	10	
K_e (h^{-1})	0.078	
$t_{1/2}$ (h)	8.86	Long half-life. Similar to IV half-life.
AUC_{0-t} (µg.h/ml)	87	
AUC (µg.h/ml)	95	To be compared with potency
$AUC_{extrapol}$ (%)	8.9	Extrapolated Area < 20%
Cl/F (ml/h/kg)	105	
V/F(ml/kg)	1345	
t_{max} (h)	4.0	Delayed absorption
C_{max} (µg/ml)	6.0	To be compared with potency
F (%)	56	Moderate Bioavailability

- IVPK: DQ2 displayed low systemic clearance (1 % MLBF), moderate Volume of distribution (~total body water (0.7 l/kg)), long $t_{1/2}$
- POPK: Delayed absorption, long $t_{1/2}$, oral bioavailability= 56 %
- IV and oral AUCs and C_{max} should be compared with *in vitro* potency to assess potential for efficacy & design of pharmacology studies.
- CL, V_{ss} data should be used in IVIVC analysis

1. *Gabrielsson J & Weiner D. Pharmacokinetic and Pharmacodynamic data analysis: Concepts & Applications. 3rd ed. Swedish Pharmaceutical Press*
2. **Davies, B.; Morris, T. Physiological parameters in laboratory animals and humans. Pharm. Res., 1993 10(7), 1093-1095.*