Xenobiotica

In vitro metabolism and in vivo pharmacokinetics of bentysrepinine (Y101), an investigational new drug for anti-HBV infected hepatitis: focus on interspecies comparison

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Table S1. Comparison of in vitro metabolic parameters in rat, dog, monkey and human liver microsomes (n = 2).

species	Phase I (+NADPH)			In vivo
	$t_{1/2}$ (min)	CL_{int} (mL/min/kg)	CL_H[a] (mL/min/kg)	CL[b] (mL/min/kg)
Dog	58.2	22.1	12.9	25.5
Monkey	182	3.66	3.38	56.8
Human	385	1.48	1.38	NA[c]

[a], The hepatic clearance (CL_H) of Y101 was obtained from in vitro data using well-stirred liver model disregarding all binding (Davies et al., 1997; De et al., 2007; Ring et al., 2011; zhang et al., 2018).

[b], the value was calculated by intravenous pharmacokinetic study in dogs and monkeys.

[c], not applicable.

References

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Table S2. The toxicokinetic parameters of Y101 in monkey plasma after oral administration of Y101 for 1 day and 14 days.

Parameters[a]	Unit	day1	day14	day1	day14
		P.O.(n=6)	P.O.(n=6)	P.O.(n=6)	P.O.(n=6)
Dose	mg/kg	30	30	100	100
C_{max}	ng/mL	1199 ± 1050	1410 ± 879	1090 ± 678	2092 ± 1651
AUC_{0-t}	ng.h/mL	2810 ± 2621	2450 ± 1163	5334 ± 555	4527 ± 2469
$AUC_{0-\infty}$	ng.h/mL	2832 ± 2644	2466 ± 1160	5441 ± 628	4549 ± 2455

[a], Sampling time points were selected at pre-dose, 0.25, 0.5, 1, 1.5, 2, 3, 4, 5, 6, 9, 12 and 24 h post dose, respectively. The toxicokinetic parameters were evaluated using non-compartmental analysis with Phoenix WinNonlin (version 6.3; Pharsight, Certara Corp, Princeton, NJ, USA).