Evaluation of Safety, PK, and PD of a Novel Proton Pump Inhibitor, YH-1885, in Healthy Volunteers

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To evaluate the safety, PK, and PD characteristics of a reversible H^+/K^+-ATPase inhibitor, YH-1885, a single-blind, randomized, placebo-controlled, parallel group study was conducted in 30 healthy volunteers. The volunteers were randomly allocated to single dose groups of 60mg, 100mg, 150mg, 200mg, and 300mg. Plasma and urine concentrations of YH-1885 and its metabolites were determined by LC/MS.

Safety and tolerability were evaluated by physical examination and clinical laboratory results. PK parameters were calculated by non-compartmental analysis. Continuous 24-hr gastric pH monitoring was conducted during the study, 24 hrs before and after drug administration. Serum gastrin levels were also measured.

Dose	Tmax(hr)	Cmax(ng/ml)	$t_{1/2}$(hr)	AUC(ng · hr/ml)	CL/F(L/hr)
60mg	2.26	78.09	2.41	363.94	200.57
100mg	1.50	168.68	2.39	667.77	201.97
150mg	2.51	266.75	2.18	1175.36	133.59
200mg	2.13	361.37	2.37	1343.06	157.60
300mg	1.39	722.41	10.63	2969.60	101.79

AUC and Cmax of YH-1885 were proportional to administered dose. Low concentrations of metabolite (M2) in plasma were detected in dose groups above 150 mg. In urine, neither YH-1885 nor any of its metabolites were recovered. Intragastric pH monitoring results showed a trend towards increased mean pH and time fraction pH>3 in relation to increasing dose. When compared with placebo group, significant changes in gastrin levels were observed after administration of YH-1885.

YH-1885 was generally safe and well tolerated for up to 300mg. YH-1885 inhibited acid secretion dose dependently. The therapeutic efficacy needs to be evaluated after multiple dosing.