

SAFETY AND PHARMACOKINETICS OF THE NON-NUCLEOSIDE POLYMERASE INHIBITOR, HCV-796: RESULTS OF A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, ASCENDING SINGLE-DOSE STUDY IN HEALTHY SUBJECTS

Priyamvada Chandra,¹ Donald Raible,¹ Lisa Moyer,¹ Dawn Harper,¹ John Speth,¹ Stephen Villano,² Richard Fruncillo³

¹Dept of Clinical Pharmacology, Wyeth Research, Collegeville, PA; ²ViroPharma, Inc., Exton, PA; ³Clinical Pharmacology Unit, Wyeth Research, Philadelphia, PA

Purpose: HCV-796 is an inhibitor of hepatitis C virus (HCV) RNA-dependent RNA polymerase that has demonstrated potent antiviral activity in vitro. The purpose of this study was to assess the safety, tolerability, and pharmacokinetics of ascending, single oral doses of HCV-796 in healthy subjects.

Methods: A phase 1, randomized, double-blind, placebo-controlled, ascending, single-dose study of orally administered HCV-796 was conducted. Healthy subjects aged 18 to 45 years received 25, 50, 100, 250, 500, 1000, or 2000 mg oral doses of HCV-796 or placebo (6 active, 2 placebo per dose group). Subjects in the 100 mg dose cohort received HCV-796 in a fasting and fed state.

Results: HCV-796 was generally well tolerated with no serious treatment-emergent adverse events. Mild to moderate headache was the most frequently reported adverse event. No subject discontinued because of an adverse event. The table below shows mean (\pm SD) HCV-796 pharmacokinetic parameters for all dose groups. When given with food, AUC increased \sim 1.4-fold.

Dose	C _{max} (ng/mL)	T _{max} (hr)	t _{1/2} (hr)	AUC (ng*hr/mL)
25 mg	48.4 \pm 13.5	4.0 \pm 1.1	6.1 \pm 2.2	528 \pm 136
50 mg	105 \pm 30.9	3.5 \pm 0.8	33.8 \pm 13.3	2854 \pm 840
100 mg (fasting)	179 \pm 38.9	3.5 \pm 0.5	41.2 \pm 22.7	4835 \pm 1464
100 mg (fed)	283 \pm 48	6.0 \pm 1.8	36.7 \pm 27.1	7070 \pm 4767
250 mg	297 \pm 131	2.7 \pm 0.5	58.4 \pm 23.9	8540 \pm 4511
500 mg	550 \pm 218	2.7 \pm 0.8	38.1 \pm 6.7	10417 \pm 3875
1000 mg	696 \pm 245	2.2 \pm 0.7	73.4 \pm 38.4	18800 \pm 7754
2000 mg	875 \pm 160	2.1 \pm 0.4	61.8 \pm 14.1	18814 \pm 6733

Conclusions: Single doses of HCV-796 were generally safe and well tolerated. It appears that AUC reaches a maximum at the 1000 mg dose of HCV-796.

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