Influence of Rifampin-mediated OATP1B1/1B3 Inhibition on the Pharmacokinetics of Clazosentan

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RESULTS – SAFETY AND TOLERABILITY

Overall, 13 of 14 exposed subjects reported 44 treatment-emergent AEs. The incidence of AEs was higher following treatment B (12 subjects, 29 AEs) compared to treatment A (7 subjects, 15 AEs).

Following i.v. infusion of clazosentan, the most common AE was headache (10 out of 14 subjects, 14 AEs) with a higher incidence in treatment B (8 subjects, 9 AEs) compared to treatment A (5 subjects, 5 AEs). The incidence and frequency of AEs commonly reported after clazosentan infuion, i.e., nausea and vomiting, were also higher following treatment B compared to treatment A. All AEs resolved without sequelae.

No clinically relevant changes in clinical laboratory, vital signs, and body weight were determined.

CONCLUSIONS

- Following administration of a single i.v. dose of rifampin, exposure to clazosentan was increased by 3 – 4 fold and Vss and CL were decreased by 2.4- and 3.9 fold, respectively. The t1/2 of clazosentan was not affected by rifampin.
- Clazosentan is a substrate of the OATP1B1/1B3 transporters
- Clazosentan (15 mg for 3h) administered after rifampin or its matching placebo was safe and tolerated