Low-Dose Rifabutin Triple Therapy (RHB-105) Demonstrates High Helicobacter pylori (H. pylori) Eradication Rates

Physiologically-Based Pharmacokinetic Modeling Supports Favorable Intragastric Rifabutin Concentrations for 50 mg Q8H Dosing vs 150 mg QD

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Based on steady state simulations, time above MIC90 for rifabutin 50 mg Q8H (RHB-105) vs Rifabutin 150 mg QD was observed to be significantly higher (p<0.001) based on the final PBPK model predictions, which suggest that the duration of intragastric rifabutin concentrations for 50 mg Q8H is much longer than for rifabutin 150 mg QD. This suggests that lower doses of rifabutin can achieve higher intragastric concentrations for a longer period, which may be effective for the eradication of H. pylori infection.

Key findings:
- Rifabutin 50 mg Q8H achieved 2.68-times longer time above MIC90 in the gastric lumen vs. rifabutin 150 mg QD.
- Without meals: rifabutin 50 mg Q8H achieved 2.73-times longer time above MIC90 in the gastric lumen vs. rifabutin 150 mg QD.
- Consistent and sustained plasma rifabutin concentrations with 50 mg Q8H are similar to the increased time above MIC90 for rifabutin 150 mg QD in the fed condition.

METHODS
- Pharmacokinetic Properties of RHB-105 from PBPK Modeling: Intragastric Rifabutin Concentrations Based on Dosing Regimes (Table 1, Figure 2)
- Consistent and sustained plasma rifabutin concentrations with 50 mg Q8H are similar to the increased time above MIC90 for rifabutin 150 mg QD in the fed condition.

RESULTS
- Plasma Rifabutin Concentrations Based on Dosing (Figure 3): RHB-105 vs Rifabutin 150 mg QD
- Consistent and sustained plasma rifabutin concentrations with 50 mg Q8H are similar to the increased time above MIC90 for rifabutin 150 mg QD in the fed condition.

CONCLUSION
- Adequate intragastric antibiotic concentrations are imperative for eradication of H. pylori.
- Dosing rifabutin at 150 mg QD does not replicate the sustained intragastric concentrations predicted when dosing rifabutin at 50 mg Q8H.
- A low-dose rifabutin 50 mg Q8H (as in RHB-105) maintains intragastric concentrations at or above the MIC90 for rifabutin 150 mg QD in the fed condition.
- There may be a link between sustained high intragastric rifabutin exposure and the high eradication rates seen with low-dose rifabutin 50 mg given Q8H (RHB-105).

REFERENCES
- Phase 3 RHB-105 studies. The final parameterized PBPK model was validated against the plasma PK data not used for fitting.
- Plasma pharmacokinetic (PK) data for rifabutin were obtained from the RHB-105 Phase 1 clinical development program for H. pylori treatment.
- The final parameterized PBPK model was validated against the plasma PK data not used for fitting.
- The PBPK model was used to predict rifabutin concentrations in the gastric lumen that would be at or above the MIC for prolonged 24-hour period at steady state based on rifabutin 50 mg Q8H and rifabutin 150 mg regimens.

CONTRAINDICATIONS
- Rifabutin is contraindicated for patients with a history of rifabutin or rifampin allergy.
- Rifabutin is also contraindicated for patients with symptomatic or asymptomatic HIV infection.