Radezolid demonstrates favorable safety compared to linezolid in a three-month rat toxicology study

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Abstract

Background: To evaluate the long-term safety of radezolid (RDZ), an investigational clinical development, a three-month rat toxicology study was undertaken. As a comparator linezolid (LNZ) was dosed in a concurrent study, doses were chosen to closely approximate exposures of either proposed (RDZ) or approved (LNZ) clinical use. Both studies have one-washout period and RG3452 determination, the ratoscorporated one-month recovery arm.

Methods: Rats (Male and Female) were dosed via oral gavage daily for three months, with a one-month scheduled interim sacrifice and a one-month recovery. LNZ was dosed via oral gavage daily for three months with a one-month scheduled sacrifice, but no recovery arm. The doses chosen for RDZ were 10, 50 and 200 mg/kg/day, and for LNZ, 40 and 100 mg/kg/day; Table 1 shows rat pharmacokinetic data for these compounds to support these dose selections.

Results:

• Male and female rats administered 100 mg/kg/day of RDZ exhibited decreased body weight and food consumption, with associated clinical signs that were constant throughout the study. These were not accompanied by changes in hematologic, clinical chemistry, and histopathology parameters.

• For LNZ, administration of 200 mg/kg/day resulted in decreased body weight and food consumption, with a decrease in body weight and food consumption observed throughout the study.

• RDZ-dosed rats had no effect on clinical observations or mortality.

• LNZ-dosed rats exhibited decreased body weight and food consumption, with associated clinical signs that were constant throughout the study.

• No changes in hematologic, clinical chemistry, or histopathology parameters were observed in LNZ-dosed rats, but body weight and food consumption were decreased throughout the study.

• No test-article-related changes in body weight or clinical signs were observed at any dose level for RDZ, resulting in a No

Conclusion: Radezolid demonstrated favorable safety compared to linezolid in a three-month rat toxicology study.

References
