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Utilizing a Clinical Utility Index in a Phase II, Randomized, Bayesian Response-Adaptive Design to Study the Efficacy and Safety of Gepotidacin (GSK2140944) in Patients with Acute Bacterial Skin and Skin Structure Infections

Background

- This Phase 2 study evaluated efficacy, safety, and pharmacokinetics of 3 IV/oral doses of GEP in subjects with suspected Gram-negative bacterial skin infections or skin and skin structure infections (SSSIs).
- The study was conducted at 19 sites in the USA from December 2015 to May 2016.
- Efficacy was assessed at primary and secondary endpoints.

Methods

- Utilizing a Clinical Utility Index in a Phase II, Randomized, Bayesian Response-Adaptive Design.
- This design incorporated an adaptive enrichment; when 31% of patients were enrolled, the trial was reconsidered to 40%. This reassessment was performed to avoid treatment with an ineffective compound.
- 19 sites in the USA, 116 patients enrolled in total.

Efficacy

- The primary endpoint was cure, which is defined as the proportion of the following efficacy and safety endpoints:
- Cure rate as defined by clinical success (defined as a 100% reduction in the local skin area of the lesion at the end of the treatment period).
- Time to clinical success, defined as the first time point that a clinical success was observed in at least 31% of patients.

Results

- The study was safe and well-tolerated, with a comparable incidence of AEs and serious AEs.
- AEs were primarily mild to moderate in severity, and the most common AEs were diarrhoea, vomiting, nausea, and headache.
- The study met the primary endpoint, with a cure rate of 97% (95% CI: 88%–99%) in the mITT population.

Conclusions

- This study demonstrates the safety and efficacy of GEP in the treatment of SSSIs.
- The study results support the further development of GEP for the treatment of SSSIs.

References


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Figure 1. Adapting to different utilities leads to a different allocation ratio. A) With threshold set at 40% utility, most patients are allocated to the 0.75 g/day dose, with a ratio of 0.75 g/day to 1.00 g/day of 1.27:1. B) With threshold set at 50% utility, there is more equal allocation of patients, with a ratio of 0.75 g/day to 1.00 g/day of 1:1. C) With threshold set at 60% utility, there is an equal allocation of patients, with a ratio of 0.75 g/day to 1.00 g/day of 1:1.