Efficacy and Safety of Rivipansel (GMI-1070) in the Treatment of Vaso-occlusive Crisis in Hospitalized Patients with Sickle Cell Disease: Results From the RESET Phase 3 Study

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OBJECTIVE
Evaluate the efficacy and safety of rivipansel for a single IV opioid exposure in hospitalized children and adults with SCD.

Study Methods and Interventions
Participants, randomized (1:1), with stratification by age and genotype, to IV rivipansel or placebo – Initiated as early as possible after decision to admit, and no later than 24 hours after the first IV opioid dose – Aged 6–11 years or weight ≤40 kg: 40 mg/kg loading dose (maximum 1680 mg), then 20 mg/kg (maximum 840 mg) every 12 hours – Aged >11 years or weight >40 kg: 40 mg/kg loading dose (maximum 1680 mg), then 20 mg/kg (maximum 840 mg) every 12 hours

Study Population
Patients aged 6-11 years with VOC who were ≥5 years of age, recruited ≥21 days after their last IV opioid exposure, and ≥12 hours after their last oral analgesic dose. Patients with active or recent pain were excluded – Median time to readiness-for-discharge, hospital discharge, and discontinuation of opioids were estimated using the log-rank analysis of covariance (ANCOVA) model, with treatment, age, and genotype as predictors.

Key Outcomes
- Primary efficacy endpoint: time from study drug initiation to the time at which each of the following readiness-for-discharge criteria were met (1) opioid discontinuation and only and pain resolution (n=362), (2) complete resolution of all symptoms as determined by the primary investigator (n=217), (3) ambulatory discontinuation and (4) blood transfusions no longer required.
- Secondary efficacy endpoints: pain in extremity, opioid use, and time to discontinuation of IV opioids.
- Efficacy analysis of primary and secondary efficacy endpoints using mixed-effects models for repeated measures and time-to-event analysis.

Study Results
- 599 patients randomized (299 rivipansel, 300 placebo).
- Demographics and baseline characteristics were well balanced between groups, except for sex and race.
- Rivipansel significantly reduced the time to readiness-for-discharge, hospital discharge, and discontinuation of IV opioids compared with placebo.

Study Conclusions
- Rivipansel significantly reduced the time to readiness-for-discharge, hospital discharge, and discontinuation of IV opioids compared with placebo.
- Rivipansel was well tolerated and demonstrated a favorable safety profile.

CONCLUSIONS
- For the secondary study population, no significant clinical or statistically meaningful efficacy signal was observed for time to readiness-for-discharge, hospital discharge, and discontinuation of opioids.
- Rivipansel significantly reduced the time to readiness-for-discharge, hospital discharge, and discontinuation of IV opioids compared with placebo.

Key points
- Rivipansel significantly reduced the time to readiness-for-discharge, hospital discharge, and discontinuation of IV opioids compared with placebo.
- Rivipansel was well tolerated and demonstrated a favorable safety profile.

REFERENCES
1. Global Blood Therapeutics, Inc. (2021) Cyclerion, NHLBI/NIH, NCTS/NIH, Pfizer Inc., and University of Pittsburgh; and has received honoraria or payment for travel and publication fees from Biogen, the Eastern Medicaid advisory board for the RESET Operational Guidance Committee.
2. For the secondary study population, no significant clinical or statistically meaningful efficacy signal was observed.
3. Rivipansel significantly reduced the time to readiness-for-discharge, hospital discharge, and discontinuation of IV opioids compared with placebo.

AUTHOR DISCLOSURES

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