Comparison Of Sustained Release Granisetron (APF530) To A Single Dose Of Palonosetron For The Prevention Of Chemotherapy-Induced Nausea And Vomiting (CINV) Following A Phase 3 Study

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Background

Prevention and control of nausea and emesis are paramount in the treatment of cancer patients. 5HT3 antagonists, as a class, have become the most common antiemetic agents used in chemotherapy-naive nausea and vomiting (CINV). APF530 is a unique 5HT3 antagonist granisetron polyglutamate (TPG-PS) that delivers a single sustained-release injection in the abdomen and contains the 5HT3 antagonist, granisetron. APF530 is designed to deliver granisetron over a 5-day period.

Methodology

Study Design: Phase 3, randomized, double-blind, placebo-controlled, parallel group study.
Participants: Chemotherapy naïve or non-naive, male or female patients, 16 years old. Patients were allowed to enroll and continue into subsequent treatment cycles regardless of the severity of nausea and/or vomiting in the previous chemotherapy cycle.

Participants received daily administrations of either moderately (MEC) or highly (HEC) emetogenic chemotherapy as defined by Hesketh et al., 1998.

Drug administration: The IV and SC injections were given concomitantly 30 to 60 minutes before chemotherapy. Placebo was saline solution for both the IV and SC injections.

Treatment groups:
- Palonosetron 0.25 mg IV and placebo SC
- Granisetron 10 mg SC and placebo IV
- Placebo was isotonic saline for both the IV and SC injections.

Primary outcomes as defined by Complete Response (CR): no episodes of nausea and no emesis requiring rescue medication.

CINV: Chemotherapy-Induced Nausea and Vomiting

Phase 3, randomized, multicenter, observer-blind, double-dummy, parallel group study.

Participants

Demographics

Overall, the C200-05 clinical study enrolled a total of 1285 patients. The total number of patients enrolled in the 2 groups is 642 and 643, respectively, in the moderate and highly emetogenic chemotherapy groups.

Ecological factors were the majority of the treatment populations, for both the HEC (63.4-63.5%) and HEC (62.8-64.1%) groups.

Reference: Granisetron was also used as an antiemetic agent in both control groups.

Conclusion

Compared to placebo, patients receiving the 10 mg dose of APF530 had numerically higher CR rates for acute, delayed, and overall CINV in patients undergoing MEC and HEC.

Safety Results

Overall, <1% of the patients discontinued for treatment-related events.

AEs were generally mild in severity and considered by the investigator to be unrelated to treatment.

There were no deaths due to treatment-related AEs or SAEs.

Efficacy Results

Figure 1: Cycle 1: Complete Response - Moderate Emetogenic Chemotherapy

Figure 2: Cycle 1: Complete Response - Highly Emetogenic Chemotherapy

PK Results

Figure 5: After a single SC administration of 10 mg APF530, granisetron was absorbed with median Tmax values of 32.7 hours. Blood levels of granisetron were obtained over the entire 5-day period.

Figure 6: Comparison of Sustained Release Granisetron (APF530) To A Single Dose Of Palonosetron For The Prevention Of Chemotherapy-Induced Nausea And Vomiting (CINV) Following A Phase 3 Study

Figure 7: Summary of Injection Site Observations Related to Treatment Safety In Cycle 1

Figure 8: Incidence of Treatment Related Adverse Events

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18 years old. Patients were allowed to enroll and continue into subsequent treatment cycles regardless of the severity of nausea and/or vomiting in the previous chemotherapy cycle.

Study drug was given in up to four chemotherapy treatment cycles.

Injection site observations occurred in up to 10% of patients, including bruising, nodules, erythema, and pain.

Related injection site reactions were mild in severity in Cycle 1, and tended to increase over multiple cycles.

Overall, <1% of the patients discontinued for treatment-related events.

AEs were generally mild in severity and considered by the investigator to be unrelated to treatment.

There were no deaths due to treatment-related AEs or SAEs.

Figure 3: Summary of Complete Response In Cycle 1 Comparing Native vs Reformulation