Phase 3 Comparison of APF530 Versus Ondansetron, Each in a Guideline-Recommended 3-Drug Regimen, for Prevention of Chemotherapy-Induced Nausea and Vomiting Due To Anthracyline + Cyclophosphamide-Based Highly Emetogenic Chemotherapy Regimens: A Post Hoc Subgroup Analysis of the MAGIC Trial

Ingrid Schadig1, Richy Agajanian2, Shaker Dakhil3, Charles Taylor4, Sharon Wilks5, William Cooper6, Michael Mosier7, Yvette Payne8, Michael Klepper9, Jeffrey Vacirca10

1Compass Oncology, U.S. Oncology Network, Tulsa, OK; 2The Oncology Institute of Hope and Innovation, Whittier, CA; 3Cancer Center of Kansas, Wichita, KS; 4Tula Cancer Institute, Tulsa, OK; 5Cancer Care Centers of South Texas, San Antonio, TX; 6TJS International, Flemington, NJ; 7EMB Statistical Solutions, LLC, Overland Park, KS; 8Heron Therapeutics, Redwood City, CA (at time of study); 9Drug Safety Navigator, LLC, Durham, NC; 10North Shore Hematology Oncology, East Setukey, NY

BACKGROUND

• Chemotherapy-induced nausea and vomiting (CINV) associated with highly emetogenic chemotherapy (HEC) adversely affects quality of life, especially in the delayed phase (24-120 h after chemotherapy), and affects chemotherapy compliance.
• Anthracyline + cyclophosphamide (AC)-based regimens, considered among the most emetogenic, are used to treat patients with advanced non-small cell lung cancer, and highly emetogenic chemotherapy (HEC) to HEC in American Society of Clinical Oncology (ASCO) 2011 emetogenicity scores.
• AC-based HEC is often administered to cancer patients, a mostly female population, with a high risk of CINV.
• Antinausea guidelines for HEC recommended a 3-drug regimen of a 5-HT3 antagonist type (1+1+1) regimen, a neurokinin-1 (NK-1) receptor antagonist, a neurokinin-1 receptor antagonist, and dexamethasone (DEX).

APF530 (granisetron injection, extended release)

• APF530 is a new formulation of 5-HT3 and a viscous borosilicate glass (triethylene glycol) polymer that undergoes controlled hydrolysis in subcutaneous (SC) tissue to provide extended release of granisetron for the prevention of both acute (0-24 h after chemotherapy) and delayed CINV
• A single SC dose of APF530 provides therapeutic concentrations of granisetron for ≥ 3 days.

METHODS

• This was a prospective, randomized, double-blind, duplicate-dose, multinational phase 3 trial (Figure 1).
• A total of 342 adult patients in the United States with histologically or cytologically confirmed non-small cell lung cancer (NSCLC) and receiving AC (as ASCO 2011 emetogenicity criteria) were enrolled.
• Patients were stratified by the presence of cisplatin ≥ 50 mg/m², and delayed CINV was recorded between days 3 and 5.
• Rescue medication was permitted at the investigator’s discretion.

Patient Population

A total of 342 NSCLC patients (161 per arm) in the ITT population received AC-based HEC (APF530 arm, 174; control arm, 168). Baseline characteristics were well balanced across both treatment arms (Table 1).

RESULTS

Efficacy

• In the AC subgroup (Table 2), delayed-phase CR numerically was higher in the APF530 arm versus the control arm. The approach was consistent (APF530 arm, 63.6%; control arm, 56.0%) with a P = 0.062.
• In the overall phase, trends in favor of the APF530 arm versus the control arm were observed, although not statistically significant: 50.1% versus 47.1% (P = 0.388).

Safety

• Consistent with the overall population, the APF530 regimen was generally well tolerated in the AC subgroup; no new safety signals were identified (Table 3).
• Most patients experienced ≤ 1 TEAE (APF530 arm, 19.5%; control arm, 16.9%).
• Excluding ISRs, the most frequently reported TEAEs were fatigue, constipation, nausea, and headache, occurring with a similar frequency in the APF530 arm compared with the control arm.

CONCLUSIONS

• APF530 is the first and only 5-HT3 receptor antagonist demonstrated superior efficacy in a 3-drug versus 3-drug phase 3 efficacy trial.

REFERENCES