Sustainability of Antiemetic Complete Responses (CRs) With APF530 (Sustained-Release Granisetron) During Multiple Cycles of Moderately (MEC) and Highly (HEC) Emetogenic Chemotherapy: Results of a Randomized Phase 3 Trial

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Abstract 9626

• Greater than 30% of chemotherapy patients experience chemotherapy-induced nausea and vomiting (CINV) despite use of the latest generation of antiemetics. Improved approaches toward antiemetic therapy are clearly needed.
• APF530 is a new polymeric formulation of 5% granisetron and a biodegradable insulin-poly(D-lactide) copolymer with electrostatic charge in which granisetron is entrapped.
• In clinical studies in patients undergoing chemotherapy, a single dose of subcutaneously administered APF530 provided sustained therapeutic drug levels for over 5 days (112 hours).
• In a phase 3 trial, APF530 500 mg SC (containing 10 mg granisetron) was demonstrated to be noninferior to palonosetron 0.25 mg IV in the control of acute and delayed CINV in patients who received MEC or HEC chemotherapy.
• Although variances occurred, APF530 500 mg SC was comparably sustained superior CR rates in setting of delayed CINV with MEC.
• The sustainability of responses is the phase 3 trial with APF530 through 4 cycles of chemotherapy was evaluated.

METHODS

• 1,683 patients scheduled to receive single doses of MEC or HEC therapy in cycle 1 were randomized to APF530 250 mg or 500 mg SC or 10 mg or 5 mg granisetron or palonosetron 0.25 mg IV. Standard doses of IV dexamethasone (8 mg IV, 20 mg HEC) were administered per protocol prior to chemotherapy on day 1; oral dexamethasone (0.25 mg IV) was given to HEC patients on days 2, 3, and 4.
• In cycle 1, 1,184 patients who received palonosetron 0.25 mg IV were randomized to APF530 250 mg or 500 mg SC (5 or 10 mg granisetron) or palonosetron 0.25 mg IV.
• Among 92 patients who received APF530 500 mg and completed 4 cycles of MEC: 57, 55, and 52 had a CR in the acute-onset, delayed-onset, and overall phases, respectively.
• The 500-mg dose generally sustained a higher CR in the delayed-onset (55, and 52 had a CR in the acute-onset, delayed-onset, and overall phases, respectively)
• Greater than 30% of chemotherapy patients experience chemotherapy-induced nausea and vomiting (CINV) despite use of the latest generation of antiemetics. Improved approaches toward antiemetic therapy are clearly needed.

RESULTS

Table 1. Patient Demographics

| Treatment | APF530 250 mg | APF530 500 mg | Placebo | Palonosetron 0.25 mg
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<tr>
<td>% Complete Treatment Response</td>
<td>63.2%</td>
<td>56.8%</td>
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<tr>
<td>% Complete Treatment Response</td>
<td>58.0%</td>
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<td>% Complete Treatment Response</td>
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<td>50.8%</td>
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Table 1. Current Chemotherapy Regimens

| Treatment | APF530 250 mg | APF530 500 mg | Placebo | Palonosetron 0.25 mg
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Sustainability of CR Rates Through Cycles 1 and 2; Cycles 1, 2, and 3; and Cycles 1, 2, 3, and 4 (Figures 2A-C and 2D)

• Acute-onset CRs (CRs 1A, 2A, 3A, and 4A) were sustained across all 4 cycles with APF530 250 mg and 500 mg SC and palonosetron 0.25 mg IV.
• CR rates of 63% (250 mg) and 57% (500 mg) with MEC and 72% (250 mg) and 63% (500 mg) with HEC in cycle 1.
• Among 92 patients who received APF530 500 mg and completed 4 cycles of MEC, 17, 18, and 17 had an CR in the acute-onset, delayed-onset, and overall phases, respectively.
• Among 10 patients who received APF530 500 mg and completed 4 cycles of MEC, 11, 12, and 12 had a CR in the acute-onset, delayed-onset, and overall phases, respectively.
• The 500-mg dose generally sustained a higher CR in the delayed-onset cycles (38, and 34 had a CR in the acute-onset, delayed-onset, and overall phases, respectively)

CONCLUSIONS

• APF530 500 mg demonstrated noninferiority to palonosetron in the prevention of CINV in the acute-onset and delayed-onset cycles following administration of emetogenic chemotherapy (MEC or HEC).
• In this subset analysis, sustainability of CR rates over multiple cycles there were no differences between APF530 250 mg and 500 mg in terms of weekly-cycle CR rates in any phase for patients receiving MEC or HEC regimens.
• Acute-onset, delayed-onset, and overall CR rates were sustained across 4 cycles of chemotherapy with MEC and HEC regimens with both APF530 210 mg and 500 mg.
• CR rates in cycle 4 were maintained at high rates in cycles 2, 3, and 4.
• CR rates tended to improve with successive cycles. A consistently higher proportion of patients who did not have a CR in cycle 1 achieved a CR in later cycles than those with a CR in cycle 1 and no CR in later cycles.
• APF530 has shown sustained activity in the prevention of CINV in first and subsequent cycles of chemotherapy in patients receiving MEC and HEC regimens.

Figure 3A–C

Sustainability of CR Rates During the Acute-Onset, Delayed-Onset, and Overall Phases in Cycles 1, 2, 3, and 4 (Figures 2A and B)

• HEC patients receiving APF530 500 mg or 10 mg granisetron + 20 mg dexamethasone had numerically superior CR rates in acute-onset, delayed-onset, and overall phases compared with placebo.
• There was a trend toward higher rates of CR with maximum cycle (in the acute-onset, delayed-onset, and overall) phases.
• Overall higher CR rates were obtained with HEC regimens compared with MEC regimens.

Cr Rates During the Acute-Onset, Delayed-Onset, and Overall Phases in Cycles 1, 2, 3, and 4 (Figures 2A and B)