

A Prospective Comparison of the Ondansetron Plus Aprepitant, Versus Ondansetron for the Prevention of Chemotherapy Induced Nausea and Vomiting

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Abstract: ***Objective:** The objective of study is to compare Ondansetron plus Aprepitant versus Ondansetron's safety for the prevention of chemotherapy induced nausea and vomiting in patients receiving Cisplatin and 5-Fluorouracil as their treatment for managing cervix cancer and head and neck cancer. **Methods:** The study was conducted in a Radiotherapy Department of tertiary care teaching hospital. Patients with cervix cancer and head and neck cancer who were scheduled to receive treatment with cisplatin and 5-fluorouracil were randomized to receive 1 of 2 treatment regimens; the standard therapy group received intravenous ondansetron 8 mg and intravenous dexamethasone 4 mg on Days 1-3. The aprepitant group received oral aprepitant 125 mg, intravenous ondansetron 8 mg, and oral dexamethasone 4 mg on Day 1; oral aprepitant 80 mg and oral dexamethasone 8 mg once daily on Days 2-3. **Results:** Of the 86 patients screened 82 were randomized. Twenty-seven (75%) of 36 patients achieved a CR in the acute phase (days 1 through 5) on the aprepitant cycle, and fourteen (32.5%) of 43 patients had a CR on the placebo cycle. In the delayed phase (days 6 through 8), 23 (64%) of the patients on the aprepitant cycle had a CR, and 21 (48.8%) of the patients on the placebo cycle achieved CR. The overall number of patients with CR for days 1 through 8 was 19 (52.7%) on the aprepitant cycle compared with 12 (27.9%) on the placebo cycle. **Conclusion:** There was a significant improvement in complete response rate with aprepitant combined with a 5HT3-RA and dexamethasone as on par with 5HT3-RA and dexamethasone alone.*

Keywords: Aprepitant, Ondansetron, chemotherapy, nausea and vomiting

1. Introduction

Although nausea and vomiting can result from surgery, chemotherapy, opiates, radiotherapy chemotherapy-induced nausea and vomiting (CINV) is potentially the most severe and most distressing. CINV may be one of the important adverse effects of treatment¹. The antiemetic therapy used for the prevention of CINV, should be tolerable in patients receiving chemotherapy, especially with highly emetic agents¹. The three categories of drugs with the highest therapeutic index for the management CINV include Type-3 5-hydroxytryptamine (5-HT3) receptor antagonists, the neurokinin-1 (NK1) receptor antagonists- Aprepitant and Fosaprepitant, and Glucocorticoids². Aprepitant is a novel neurokinin 1 (NK1) antagonist that has been shown to improve safety of anti-emetic therapy when added to a standard antiemetic regimen of a 5-hydroxytryptamine-3 antagonist³. Several studies have established that addition of a neurokinin-1 receptor antagonist (NK1-RA), such as aprepitant, to a 5-hydroxytryptamine-3 receptor antagonist (5HT3-RA) and dexamethasone can improve prevention of CINV in patients receiving highly emetogenic chemotherapy with cisplatin combination chemotherapy. We are looking out to evaluate safety of Aprepitant plus Ondansetron when compared to Ondansetron in cancer patients receiving emetogenic chemotherapy.

Background

Aprepitant is a novel neurokinin 1 (NK1) antagonist that has been shown to improve control of chemotherapy-induced nausea and vomiting (CINV) when added to a standard antiemetic regimen of a 5-hydroxytryptamine-3 antagonist plus a corticosteroid.

Objective

The objective of study is to compare Ondansetron plus Aprepitant versus Ondansetron's safety for the prevention of chemotherapy induced nausea and vomiting in patients receiving Cisplatin and 5-Fluorouracil as their treatment for managing cervix cancer and head and neck cancer.

2. Methods

The study was conducted in a Radiotherapy Department of a tertiary care teaching hospital. The study method involves choosing the patients according to the inclusion and exclusion criteria from whom an informed consent was taken. The main outcome measures will be the occurrence of vomiting, severity of nausea and tolerability of drugs. The information is collected through a data collection form from the patient's prescription and the collected data is tabulated and analyzed using suitable statistical tools.

Patients with cervix cancer and head and neck cancer who were scheduled to receive treatment with cisplatin and 5-fluorouracil were randomized to receive 1 of 2 treatment regimens; the standard therapy (placebo) group received intravenous ondansetron 8 mg and intravenous dexamethasone 4 mg on Days 1-3. The aprepitant group received oral aprepitant 125 mg, intravenous Ondansetron 8 mg, and oral dexamethasone 4 mg on Day 1; oral aprepitant 80 mg and intravenous dexamethasone 8 mg once daily on Days 2-3; Patients recorded episodes of emesis, use of rescue therapy, and severity of nausea in a diary.

Inclusion Criteria

- Cancer patients of age more than 18 years admitted in radiation oncology department.
- Patients who are receiving Cisplatin and 5-Fluorouracil therapy
- Patients with cervix cancer and head and neck cancer
- Patients who are willing to participate.

Exclusion Criteria

- Cancer patients of age less than 18years
- Patients who are not willing to participate in the study.

3. Results

Of the 86 patients screened 82 were randomized. Of these, 4 patients were excluded from the safety and efficacy analyses because they did not receive both cisplatin and at least 1 dose of study drug. The median age was 33 years (range, 16 to 62 years). Fig.1 shows gender wise distribution of patients in which 50 females and 29 males are taken and randomly distributed into apripitant and placebo groups.

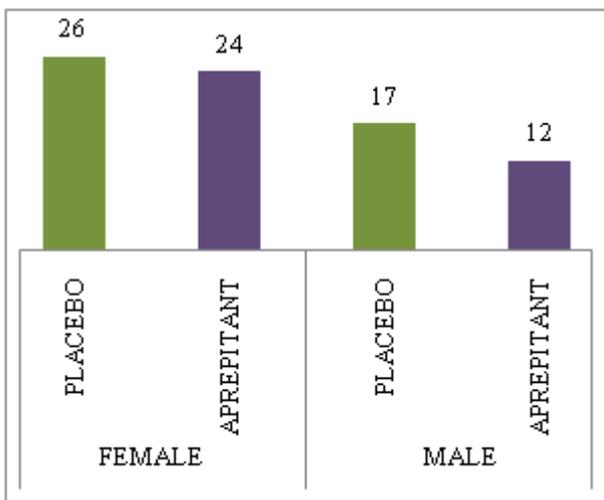
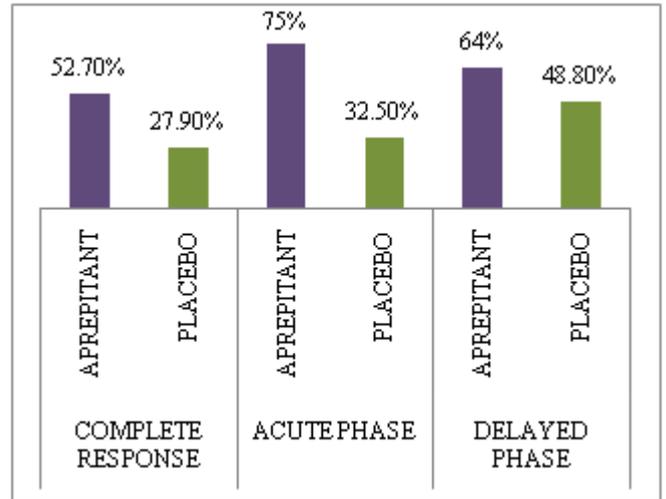


Figure 1: Gender Wise Distribution of Patients

Twenty-seven (75%) of 36 patients achieved a CR in the acute phase (days 1 through 5) on the apripitant cycle, and fourteen (32.5%) of 43 patients had a CR on the placebo cycle. In the delayed phase (days 6 through 8), 23 (64%) of the patients on the apripitant cycle had a CR, and 21 (48.8%) of the patients on the placebo cycle achieved CR. The overall number of patients with CR for days 1 through 8 was 19 (52.7%) on the apripitant cycle compared with 12 (27.9%) on the placebo cycle. Aprepitant group had very good response in acute and delayed phases of chemotherapy as on par with the placebo group.



The Fig.2 showing percentage patients with complete response from day 1 to 8, and also in both acute and delayed phases of chemotherapy.



Figure 3: Number of Episodes of Vomitings In Acute Phase

Fig.3 depicts number of episode of vomitings in acute phase of apripitant Vs placebo groups. Patients who are experiencing less (0-1) episode of vomitings are more with apripitant therapy i.e. 75% (n=27) compared to placebo group i.e. 32.6% (n=14). Patients who had more than 2 episodes are much higher in placebo group when compared with apripitant group. No patient had experienced more than 5 episodes in apripitant group whereas it is seen in placebo group i.e. 7% (n=3) had 6-7 episodes and 18.6% (n=8) had more than 7 episodes.

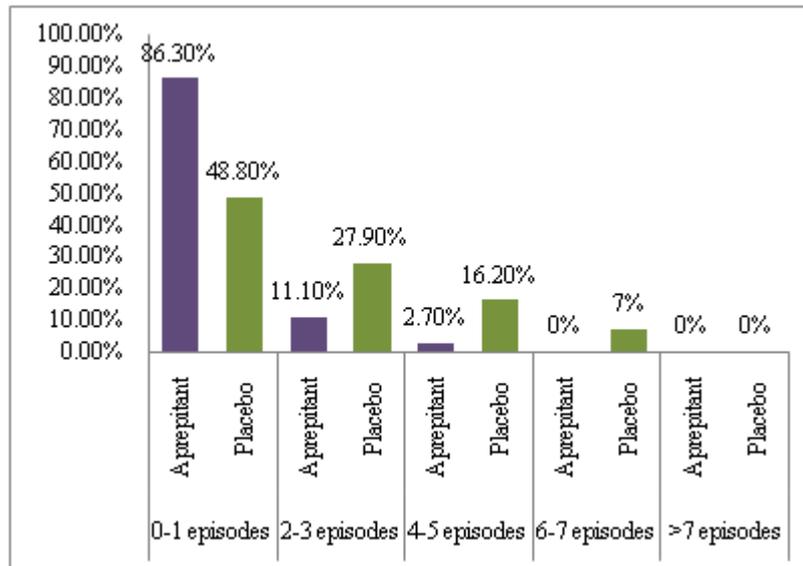


Figure 4: Number of Episodes of Vomitings in Delayed Phase

Fig.4 depicts number of episode of vomitings in delayed phase of aprepitant Vs placebo groups. Patients who are experiencing less (0-1) episode of vomitings are more with aprepitant therapy i.e. 86.3% (n=31) compared to placebo group i.e. 48.8% (n=21). Patients who had more than 2 episodes are much higher in placebo group when compared with aprepitant group. No patient had experienced more than 5 episodes in aprepitant group whereas it is seen in placebo group i.e. 7% (n=3) had 6-7 episodes. Both the groups did not experience more than 7 episodes of vomitings in delayed phase.

4. Discussion

Patients in this trial received a chemotherapy of cisplatin and 5 fluorouracil combination. The current analysis evaluated whether the aprepitant combination with 5-HT₃ receptor antagonist and dexamethasone is beneficial over standard 5-HT₃ receptor antagonist and dexamethasone regimen in chemotherapy induced nausea and vomiting's. In our study we concluded that Twenty-seven (75%) of 36 patients achieved a CR in the acute phase (days 1 through 5) on the aprepitant cycle, and fourteen (32.5%) of 43 patients had a CR on the placebo cycle. In the delayed phase (days 6 through 8), 23 (64%) of the patients on the aprepitant cycle had a CR, and 21 (48.8%) of the patients on the placebo cycle achieved CR. The overall number of patients with CR for days 1 through 8 was 19 (52.7%) on the aprepitant cycle compared with 12 (27.9%) on the placebo cycle.

In a study A total of 523 patients were evaluated for efficacy, and 568 patients were evaluated for safety. During the 5 days after chemotherapy, the percentages of patients who achieved a complete response were 62.7% in the aprepitant group (163 of 260 patients) versus 43.3% in the standard therapy group (114 of 263 patients). For Day 1, the complete response rates were 82.8% for the aprepitant group and 68.4% for the standard. For Days 2–5, the complete response rates were 67.7% in the aprepitant group and 46.8% in the standard therapy group.

5. Conclusion

The current analysis of 82 cancer patients reveals that the use of combination therapy (oral aprepitant, intravenous ondansetron and dexamethasone) proved to be more efficacious than the placebo therapy (intravenous ondansetron and intravenous dexamethasone). There was a significant improvement in complete response rate with aprepitant combined with a 5HT₃-RA and dexamethasone as on par with 5HT₃-RA and dexamethasone alone.

References

- [1] Winnie Yeo, F. K. F. Mo, A randomized study of aprepitant, ondansetron and dexamethasone for chemotherapy-induced nausea and vomiting in Chinese breast cancer patients receiving moderately emetogenic chemotherapy; Breast Cancer Research and Treatment; February 2009, Volume 113, Issue 3, pp 529-535.
- [2] Poli-Bigelli S1, Rodrigues-Pereira J. Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomized, double-blind, placebo-controlled trial in Latin America; Cancer. 2003 Jun 15;97(12):3090-8.
- [3] Paul J. Hesketh, Steven M. Grunberg, Richard J. Gralla, David G. The Oral Neurokinin-1 Antagonist Aprepitant for the Prevention of Chemotherapy-Induced Nausea and Vomiting: A Multinational, Randomized, Double-Blind, Placebo-Controlled Trial in Patients Receiving High-Dose Cisplatin—The Aprepitant Protocol 052 Study Group; J Clin Oncol 21:4112-4119. 2003 by American Society of Clinical Oncology.