Evaluating the utilization of fosaprepitant for the treatment of breakthrough chemotherapy-induced nausea and vomiting: a retrospective analysis

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Background

- Aprepitant, and its pro-drug fosaprepitant, is an antiemetic that prevents acute and delayed vomiting by inhibiting substance P/neurokinin 1 (NK_1) receptors. Emend® is usually given in combination with 5-HT_3 antagonists and/or dexamethasone in moderate and highly-emetogenic chemotherapy. [1]
- While studies have shown the addition of NK_1 inhibitors decreases chemotherapy-induced nausea and vomiting in the acute (0-24 hours) and delayed (25-120 hours) phases, the efficacy begins to wane in the delayed with, with 68-75% efficacy compared to 83-89% efficacy in the acute phase. [2]
- According to NCCN guidelines, multiple agents can be administered for breakthrough nausea/vomiting. [3] However, no studies have been published regarding the use of NK_1 inhibitors in this setting, despite limited use in practice.
- The purpose of this study was to determine if fosaprepitant was effective if given in the breakthrough setting.

Study Objectives

- The primary objective: Determine if administering fosaprepitant for breakthrough CINV improved rates of nausea/vomiting.
- Secondary Objectives: Assessing impact of fosaprepitant on subjective rating of nausea at 24 48, and 72 hours after administration, evaluation of episodes of emesis before and after administration, evaluation of PO intake prior to and after administration, and assessment of days of nausea/vomiting before administration.

Methods

- Retrospective chart review of electronic medical records on patients who received fosaprepitant not apart of CINV protocol from January 1, 2015 to December 31, 2015.
- Evaluation for effectiveness based upon daily physician progress reports, documented Ins & Outs, documented episodes of emesis prior to and after administration, and analysis of antiemetic medications administered prior to and after administration.
- Inclusion Criteria: Patients 18 years and older admitted to WVU Medicine in Morgantown, West Virginia, whom received fosaprepitant not apart of preventative CINV therapy.
- Exclusion Criteria: Patients whom received fosaprepatant for any reason other than breakthrough CINV, outpatient fosaprepatant administration, and N/V which was not from, or cannot be concluded, from chemotherapy.

Results

- A total of 81 patients received IV fosaprepitant on 119 admissions. After inclusion and exlusion criteria, 34 patients on 41 admission were administered fosaprepitant for breakthrough CINV. In all, 36 of 41 patients were receiving chemotherapy for a hematologic malignancy. Figure 1 and Table 1 provide the demographics and breakdown of disease states

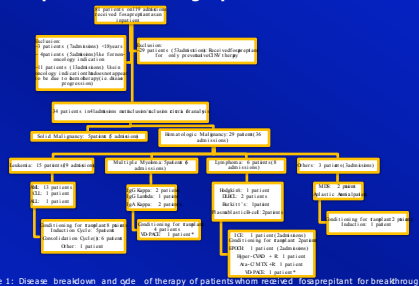
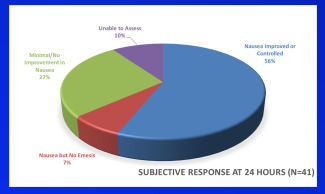


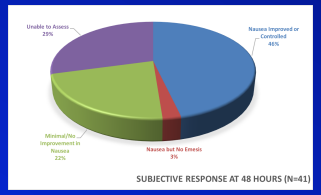
Figure 1: Disease breakdown and cycle of therapy of patients whom received fosaprepitant for breakthrough N/V
* Patient had recurrent multiple myeloma in addition to newly diagnosed lymphoma

Demographics of Patient Population	
Sex	
Male	15
Female	19
Average Age (years)	
Male	43 (21-71)
Female	49 (25-66)
Disease	
Solid Malignancy	4
Hematologic Malignancy	29
Emetogenic Risk of Cycle^	
High	15
Moderate	24
Low	5
Minimal	0
Preventative Medication Per Cycle	
NK1 inhibitor	7
Corticosteroids	23
5-HT3 antagonist	9
Other	1

Table 1: Patient demographics of those meeting indusion criteria
^Emetogenic risk based on NCCN guidelines

- **Primary Outcome**: In 78% (n=31) of chemotherapy cycles, patients reported overall improvement in Nausea/Vomiting within 72 hours of administration. Of the remaining 10 patients, 4 were unable to assess due to administration of fosaprepitant at discharge, 5 patients experienced no improvement, and 1 patient showed initial improvement but N/V worsened due to deteriorating health conditions.
- **Secondary Outcomes**: Subjective rating of displayed that a majority had nausea resolved, improvement in nausea, or nausea controlled through medications. Even those with minimal improvement at 24 and 48 hours (n=6 and n=4) improved by 72 hours (n=2). All patients (n=5) that had no improvement after 24 hours had no improvement at the end of 72 hours. (Figure 2)





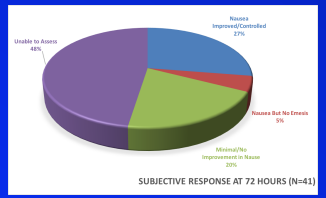


Figure 2: Subjective response of nausea at 24, 48, and 72 hours after fosaprepitant administration for breakthrough N/V. Subjective response at 48 and 72 hours had a physician progress note for that day.

Results (continued)

- Patients during 24 cycles experienced at least one episode of emesis prior to fosaprepitant; 83% (n=20) did not have any additional emesis after fosaprepitant administration. PO intake could not be assessed due to inconsistencies od documentation by nursing
- A median of 3 days of nausea (1-15 days) occurred before fosaprepitant was administered for CINV. A review of breakthrough medications used prior to and 24 hours after fosaprepitant administration is reviewed in Table 2.

Medications Used for Breakthrough CINV	Used as Breakthrough Therapy Prior to Fosaprepitant Administration	Average Amount Used Prior to Fosaprepitant administration	Used as Breakthrough Therapy Up To 24 hours After Fosaprepitant Administration	Average Amount Used Up To 24 hours After Fosaprepitant Administration
Zofran (ondansetron)				
4 mg	11	12 mg (4-48 mg)	9	9.6 mg (4-16 mg)
8 mg (PRN)	9	36 mg (8-176 mg)	3	20.8 mg (8-32 mg)
8 mg (Scheduled)	9	160 mg (40-248 mg)	2	26 mg (24-32 mg)
16 mg	0	--	0	--
Phenergan (promethazine)				
12.5 mg	25	94.5 mg (12.5-175 mg)	11	21 mg (12.5-50 mg)
25 mg	7	129 mg (25-400 mg)	3	83 mg (25-150 mg)
Compazine (prochlorperazine)				
5 mg*	2	60 mg (5-115 mg)	2	20 mg (15-25 mg)
10 mg	7	12 mg (10-30 mg)	1	--
Reglan (metoclopramide)				
10 mg	1	10 mg	1	--
25 mg	1	25 mg	1	--
Ativan (lorazepam)				
0.5 mg	29	2.8 mg (0.5-8.5 mg)	11	0.94 mg (0.5-1.5 mg)
1 mg	2	2 mg (1-3 mg)	2	1 mg
2 mg	1	2 mg	1	--
Zyprexa (olanzapine)				
5 mg	4	10 mg (5-15 mg)	2	10 mg
Reglan (metoclopramide)				
10 mg	2	90 mg (10-170 mg)	1	20 mg
Decadron (dexamethasone)				
10 mg	1	20 mg	1	20 mg
4 mg	2	8 mg	1	8 mg
2 mg	1	4 mg	1	--
Ativan (lorazepam)				
2 mg	1	2 mg	1	--
Marinol (dronabinol)				
5 mg	0	--	1	5 mg

Table 2: Evaluation of breakthrough CINV medications prior to and 24 hours after fosaprepitant administration. A median of 2 dosses of agents (range: 0-5) were given for breakthrough CINV prior to fosaprepitant administration.
* 5mg prochlorperazine was scheduled for one patient

Discussion

- Only 7 of the 39 moderately/highly emetogenic cycles received fosaprepitant as part of the preventative therapy. While NCCN guidelines recommend the addition of fosaprepitant, concerns of drug interactions and potential drug toxicity was the reason for those not to receive up front and why it was given in the breakthrough setting.
- Addition of fosaprepitant decreased both number of breakthrough agents used and amount, potentially decreasing side-effects from these medications.

Conclusion

- Fosaprepitant appears to be effective in the setting of breakthrough CINV, especially for previous emetogenic episodes.
- A randomized, prospective study appears to be warranted to determine true benefit of fosaprepitant in breakthrough CINV setting.

Disclosure: Authors have no conflicts of interest to disclose.
References: available upon request