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Comparison of an aprepitant regimen with a multiple-day ondansetron regimen, both with dexamethasone, for antiemetic efficacy in high-dose cisplatin treatment

H. J. Schmoll[1]*, M. S. Aapro[2], S. Poli-Bigelli[3], H.-K. Kim[4], K. Park[5], K. Jordan[1], J. von Pawel[6], H. Giezek[7], T. Ahmed[8] & C. Y. Chan[9]

[1]*Martin Luther University Halle/Wittenberg, Halle/Saale, Germany;* [2]*IMO Clinique de Genolier, Genolier, Switzerland;* [3]*Instituto de Oncologia Hematologia, Universidad Central de Venezuela, Caracas, Venezuela;* [4]*Medical Oncology, St. Vincent's Hospital, The Catholic University of Korea, Suwon, Korea;* [5]*Division of Hematology/Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea;* [6]*Asklepios Fachkliniken, Centre for Pneumology and Thoracic Surgery, Gauting, Germany;* [7]*Merck Research Laboratories, Brussels, Belgium;* [8]*Merck Research Laboratories, West Point, Pennsylvania, USA;* [9]*Merck & Co., Inc., Whitehouse Station, New Jersey, USA*

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Background: We compared an aprepitant regimen with a control regimen of ondansetron + dexamethasone given for 4 days.

Patients and methods: Patients scheduled to receive cisplatin ≥70 mg/m^2 were randomized to either the aprepitant regimen (aprepitant, ondansetron and dexamethasone on day 1; aprepitant and dexamethasone on days 2–3; dexamethasone on day 4) or control regimen (ondansetron + dexamethasone on days 1–4). Patients recorded vomiting, nausea and rescue therapy use. The primary end point was complete response (no vomiting and no use of rescue therapy) in the overall phase (days 1–5 post-cisplatin).

Results: Complete response rates were higher in the aprepitant than control group in the overall (72% versus 61%; $P = 0.003$), acute (day 1; 88% versus 79%; $P = 0.005$) and delayed phases (days 2–5; 74% versus 63%; $P = 0.004$), as were rates of no vomiting (overall 77% versus 62%, $P \leq 0.001$; acute 89% versus 81%, $P = 0.004$; delayed 79% versus 64%, $P \leq 0.001$). Rates of no rescue therapy were similar between groups.

Conclusions: Compared with an antiemetic regimen in which ondansetron + dexamethasone were given for 4 days, the aprepitant regimen was superior in the acute, delayed and overall phases of chemotherapy-induced nausea and vomiting. The aprepitant regimen should be considered a new standard of antiemetic therapy for cisplatin-treated patients. www.ClinicalTrials.gov Identifier: NTC00090207

Key words: aprepitant, chemotherapy, cisplatin, dexamethasone, emesis, ondansetron

introduction

The serotonin [5-hydroxytriptamine-3 (5-HT$_3$)] receptor antagonists (RAs) significantly advanced antiemetic therapy for cancer patients, but despite treatment with a 5-HT$_3$ RA plus a corticosteroid according to published guidelines [1], more than 50% of patients still vomit in response to highly emetogenic chemotherapy, such as high-dose cisplatin. The 5-HT$_3$ RAs prevent vomiting in the first 24 h after chemotherapy, i.e. the acute phase, in 73%–92% of cisplatin-treated patients when coadministered with steroids [2], but they appear to lack efficacy in the delayed phase, i.e. >24–120 h after the start of chemotherapy [3–9]. Although antiemetic guidelines in effect at the start of the current study [1] recommended that cisplatin-treated patients should receive a corticosteroid with a 5-HT$_3$ RA (or with metoclopramide) for delayed vomiting, combinations such as dexamethasone plus either ondansetron or metoclopramide have only provided complete response (no vomiting and no use of rescue therapy) in approximately 60% of patients during the delayed phase [6].

Whereas acute vomiting is known to depend primarily on serotonin, the pathophysiology of delayed vomiting is less well understood and multiple mechanisms may contribute [6]. Neurokinin-1 (NK$_1$) receptors are found in brain regions critical to regulating the vomiting reflex and a recent analysis of studies suggested a possible predominance of NK$_1$-related mechanisms during delayed-phase vomiting [10]. Aprepitant is a selective, high-affinity NK$_1$ receptor antagonist. In patients receiving highly emetogenic chemotherapy, a regimen

Correspondence to: Prof. H. J. Schmoll, Martin-Luther-University Halle/Wittenberg, Department of Internal Medicine IV, Ernst-Grube-Str.40, 06120 Halle/Saale, Germany. Tel: +49-345/557-2924; Fax: +49-345/557-2950; E-mail: hans-joachim.schmoll@medizin.uni-halle.de

combining aprepitant with ondansetron plus dexamethasone on day 1, before chemotherapy, improved complete response rates by 11–14 percentage points in the acute phase and aprepitant plus dexamethasone improved complete response rates by 20 percentage points in the delayed phase [11–13].

These previous studies compared the aprepitant regimen with a control regimen in which ondansetron and dexamethasone were given on day 1 and dexamethasone alone was given on days 2–4 [11–13]. A common clinical practice is to treat patients with a combination of a 5-HT_3 RA and a corticosteroid for multiple days. This is the first study to compare the aprepitant regimen with a multiple-day ondansetron + dexamethasone regimen similar to that used in clinical practice in patients receiving their first cycle of cisplatin chemotherapy. The primary hypothesis was that the aprepitant regimen would provide complete response (no vomiting and no use of rescue therapy) over days 1–5 post-cisplatin (overall phase) in a higher percentage of patients than the control regimen. Secondary hypotheses were that the aprepitant regimen would be superior to the control in the percentages of patients with (a) complete response during days 2–5 post-cisplatin (delayed phase) and (b) no vomiting during the overall and delayed phases.

patients and methods

design

Aprepitant protocol 801, funded by Merck & Co., Inc., was a randomized, double-blind, parallel-group trial with sponsor blinding conducted at 56 investigator sites in Europe, North America, South America and Korea. Patients gave written informed consent. The protocol was approved by the appropriate ethical review boards and the study was conducted in accordance with the principles of the Declaration of Helsinki.

patients

Cisplatin-naïve patients ≥18 years old with confirmed solid malignancies were eligible if they were scheduled for chemotherapy that included cisplatin ≥70 mg/m^2 in cycle 1. Patients were required to have a Karnofsky score ≥60 and a life expectancy of ≥3 months. Women of childbearing potential had to have a negative β-hCG pregnancy test. Exclusion criteria included planned receipt of concomitant stem cell rescue therapy or planned receipt of multiple-day cisplatin in cycle 1. Moderately or highly emetogenic chemotherapy was permitted only on the same day as the cisplatin infusion, but not within 6 days before or 6 days after cisplatin infusion. For agents of low emetogenic potential, timing of administration was not restricted, except a taxol could only be given on the same day as cisplatin. Exclusion criteria also included the following: receipt of 5-HT_3 RAs within 48 h of day 1; radiation therapy to the abdomen or pelvis any time from 1 week before day 1 to day 6; active infection; a symptomatic primary or metastatic CNS malignancy; any uncontrolled disease other than malignancy that the investigator determined might pose an unwarranted risk; vomiting and/or dry heaves/retching 24 h before cisplatin; or abnormal laboratory values [absolute neutrophil count <1500/mm^3, white blood cell count <3000/mm^3, platelet count <100, 000/mm^3, aspartate aminotransferase >2.5 × upper limit of normal (ULN), alanine aminotransferase >2.5 × ULN, bilirubin >1.5 × ULN, or creatinine >1.5 × ULN].

treatments and assessments

Patients received either the aprepitant or the control regimen in a 1:1 ratio according to a sponsor-supplied, computer-generated, random allocation schedule. Patients were stratified according to emetogenic chemotherapy (Hesketh level ≥3) received in addition to cisplatin. Study regimens were administered in a triple-dummy fashion with matching placebos. In the aprepitant regimen, oral aprepitant was given on days 1–3 (day 1, 125 mg 1 h before cisplatin; days 2–3, 80 mg); ondansetron was given on day 1 only (day 1, 32 mg i.v. infused over 15 min at 30–60 min prior to cisplatin; days 2–4, oral placebo twice daily); and oral dexamethasone was given on days 1–4 (day 1, 12 mg 30 min before cisplatin; days 2–4, 8 mg in the morning and placebo in the evening). In the ondansetron + dexamethasone regimen, aprepitant placebo was given on days 1–3; ondansetron was given on days 1–4 (day 1, 32 mg i.v. infused over 15 min at 30–60 min prior to cisplatin; days 2–4, 8 mg orally twice daily); and oral dexamethasone was given on days 1–4 (day 1, 20 mg 30 min before cisplatin; days 2–4, 8 mg twice daily). Because aprepitant has been shown to increase dexamethasone levels approximately two-fold via a CYP3A4 interaction [14, 15], the dose of dexamethasone was reduced in the aprepitant regimen to ensure similar plasma levels between the treatment groups. Patients who received a taxol were to be premedicated with dexamethasone 20 mg at 12 h and at 6 h before taxol administration and were not to receive any additional dexamethasone on day 1. Cisplatin was infused intravenously over ≤3 h.

From the start of cisplatin infusion (0 h) to the completion of day 5, patients recorded episodes of vomiting or retching/dry heaves, daily nausea using a validated 100-mm horizontal visual analog scale and rescue medication use in a diary. Rescue therapy permitted for nausea or vomiting included 5-HT_3 RAs, phenothiazines, butyrophenones, benzamides, domperidone, cannabinoids, systemic corticosteroids and benzodiazepines. Patients taking rescue therapy were considered treatment failures.

Tolerability assessments included physical examination, vital signs, 12-lead electrocardiogram and laboratory tests, including hematology, chemistry, urinalysis and pregnancy tests. Laboratory tests were performed within 1 week before day 1, at the post-treatment visit (days 6–8) and at the final follow-up visit (days 19–29). The study site investigator determined whether an adverse event was possibly, probably, definitely or not related to the study drug. During the diary period, nausea and vomiting were not considered adverse events unless they caused hospitalization, in which case they were defined as serious adverse events. After the diary period, i.e. after the morning of day 6, nausea and vomiting were captured as adverse events. Adverse events were monitored from prestudy (days –28 to –1) through to the final follow-up visit (days 19–29).

statistical analysis

The primary efficacy hypothesis was that the aprepitant regimen would be superior to the control regimen in the proportion of patients with complete response, defined as no vomiting and no use of rescue therapy, in the overall phase (days 1–5 post-cisplatin). No vomiting was defined as no vomiting, retching or dry heaves. Secondary hypotheses stated that the aprepitant regimen would be superior to the control regimen in the proportion of patients with (a) complete response in the delayed phase (days 2–5 post-cisplatin), (b) no vomiting in the overall phase and (c) no vomiting in the delayed phase. With a sample size of 175 evaluable patients per treatment regimen, the study had 96% power to detect a treatment difference of 20% in complete response (70% for aprepitant versus 50% for ondansetron), assuming a two-sided test and an overall significance level of 0.05.

The efficacy analyses used a modified intention-to-treat (mITT) population, i.e. patients who received cisplatin, took one or more doses

of study drug and had one or more post-treatment measurements. The primary efficacy end point was the percentage of patients reporting complete response in the overall phase. Secondary end points were the percentage of patients with (a) complete response in the delayed phase, (b) no vomiting in the delayed phase and (c) no vomiting in the overall phase. Exploratory end points included percentage of patients with complete response in the acute phase (day 1, i.e. 0–24 h post-cisplatin); no vomiting in the acute phase; and no significant nausea (defined as <25 mm on a visual analog scale) in the overall phase; and time to first vomiting episode in the overall phase.

Treatment comparisons of percentages of patients were made using logistic regression models that included terms for geographic region, use of concomitant emetogenic chemotherapy, gender and treatment, with *P* values directly linked to the odds ratio. Consistency of treatment effect across geographic region, use of concomitant emetogenic chemotherapy and gender were assessed by testing the interactions with treatment in the context of logistic regression models. Kaplan–Meier curves were plotted to analyze time to first vomiting episode and a stratified log-rank test was used to compare treatments. No multiplicity adjustments were made for the primary analysis because there was only one comparison during one time period. Multiplicity adjustments were made for the secondary variables to ensure a global type-I error rate ≤0.05.

The primary safety hypothesis was that the aprepitant regimen would be well tolerated in the first cycle of chemotherapy. Tolerability analyses included all patients who received cisplatin and a dose of study drug. Tolerability evaluations were based on clinical and laboratory adverse events that occurred after the start of treatment and within 14 days after treatment ended. Percentages of patients with at least one adverse event, a drug-related adverse event, a serious adverse event and an adverse event resulting in study discontinuation were summarized and compared between treatment groups using Fisher's exact test. In addition, 95% confidence intervals (CIs) for treatment differences in proportions were computed. No multiplicity adjustments were made for the tolerability analysis; therefore, *P* values should be interpreted with caution.

results

patients

Patients were enrolled from 2 January 2004 and followed up until 30 September 2004. Of 516 patients screened, 489 were randomly assigned to treatment (Figure 1). The primary efficacy analyses excluded five patients (one aprepitant, four ondansetron) because they received no study drug and/or no

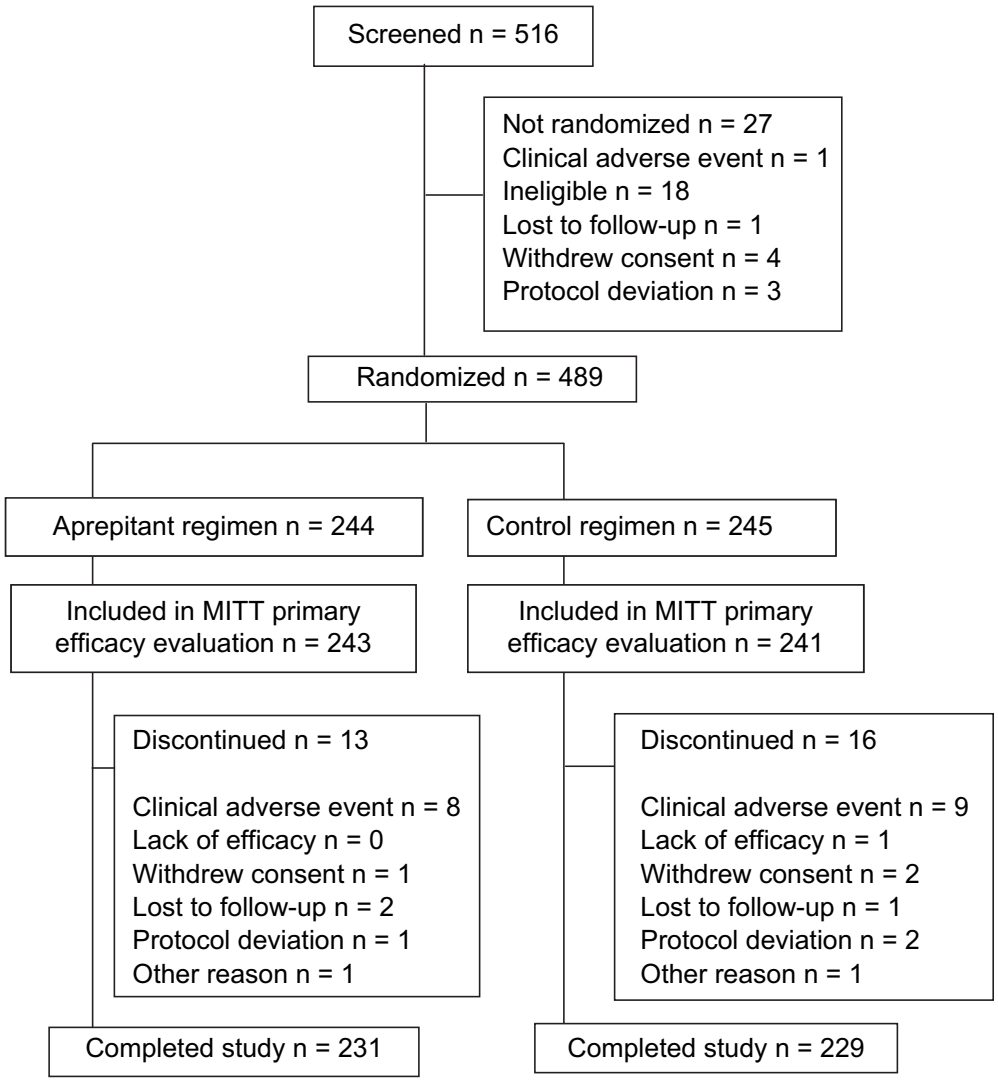

Figure 1. Study flow chart.

cisplatin or had no primary efficacy data. Baseline and demographic characteristics were generally similar between the treatment groups (Table 1).

Efficacy

The aprepitant regimen was superior to the control regimen in the percentage of patients with complete response in the overall phase [72% versus 61%, odds ratio (OR) 1.80, $P = 0.003$] as well as in the acute and delayed phases (Table 2). The treatment effect was consistent across subgroups [age, gender, race, Korean race, geographic region (Europe/America/Korea) and use of concomitant emetogenic chemotherapy].

For the individual components of complete response, the aprepitant regimen was superior to control for no vomiting in all three phases, with a 15% difference between groups in the delayed phase and the aprepitant regimen had numerically higher rates of no use of rescue therapy in all three phases (Table 2).

For complete response, no vomiting and no use of rescue medication, there were no significant interactions between treatment and either gender or geographic region in the acute, delayed or overall phases. For the end point of no vomiting during the delayed and overall phases, a significant interaction between treatment and use of concomitant emetogenic chemotherapy was detected; however, application of Gail and Simon's test showed that the numerical differences in treatment effects between strata were all in the same direction and, thus, were not qualitative in nature for either the delayed ($P = 0.343$) or overall ($P = 0.358$) phases. No additional treatment interactions for any end point and use of concomitant emetogenic chemotherapy in any phase were detected.

The aprepitant regimen provided a higher rate of protection against significant nausea in the overall, acute and delayed phases than the control regimen (Table 2), but the results were not statistically significant. There were no significant interactions between treatment and either gender, use of concomitant emetogenic chemotherapy, or geographic region in the acute, delayed or overall phases for this end point.

The Kaplan–Meier curves show that the time to first vomiting episode was significantly longer in the aprepitant group than in the control group ($P \leq 0.001$, stratified log-rank test; Figure 2) and that the percentage of patients with no vomiting at the completion of day 5 was 15% higher in the aprepitant group. Almost all first vomiting episodes occurred within the first 72 h after cisplatin infusion for both treatment groups. The Kaplan–Meier curves began to show a visual separation at 10 h and statistically significant separation at 21 h ($P < 0.05$, backwards log-rank procedure, *post hoc* analysis).

Table 1. Baseline characteristics by treatment group

	Aprepitant regimen $N = 244$	Control regimen $N = 245$
Men (%)	61	65
Women (%)	39	35
Age (years)		
Mean ± SD	59±11	58±11
Range	20–79	23–82
Race (%)		
Asian	17	18
Black	3	3
Hispanic	13	12
White	61	61
Other	6	6
Received concurrent emetogenic chemotherapy (%)[a]	10	10
Cisplatin dose		
70 to <100 mg/m^2 (% of patients)	75	74
Mean dose ± SD (mg/m^2)	78±10	78±10
Alcoholic drinks/week (% of patients)[b]		
0	71	67
1–7	18	23
>7	11	11
History (%)		
Motion sickness	5	6
Vomiting associated with pregnancy[c]	30	23
CINV	4	6
Primary cancer diagnosis (%)		
Respiratory	43	47
Urogenital	21	17
Gastrointestinal	12	12
Eyes/ears/nose/throat	10	10
Other	14	14

SD, standard deviation; CINV, chemotherapy-induced nausea and vomiting.

[a]Hesketh level ≥3.

[b]$N = 241$ for aprepitant regimen, $N = 240$ for control regimen.

[c]Percentage of women with pregnancy-associated vomiting out of a total of 96 women in the aprepitant group and 84 in the control group.

tolerability

Two patients (one aprepitant, one ondansetron) were excluded from the tolerability analyses because they did not receive cisplatin and/or study drug. The treatment groups were similar in the proportions of patients with one or more clinical adverse events, drug-related clinical adverse events and serious clinical adverse events and the incidence of discontinuations due to clinical adverse events (Fisher's exact test, $P > 0.05$) (Table 3). Overall, there was no statistically significant between-treatment difference in the incidence of any specific clinical adverse event, except for stomatitis (4.9% aprepitant versus 1.2% control, 95% CI for the difference 0.7–7.4), peripheral edema (0.4% aprepitant versus 3.7% control, 95% CI for the difference –6.5 to –1.0) and urinary tract infection (3.7% aprepitant versus 0.8% control, 95% CI 0.3–6.2). Adverse events resulting in death occurred in 12 patients (five aprepitant, seven control); no death was considered by the investigator to be related to the study drug. Serious adverse events considered by the investigator to be possibly, probably or definitely related to the study drug were upper abdominal pain in one patient in the aprepitant group, overdose in a different

Table 2. Comparison of efficacy endpoints by treatment group

	Aprepitant regimen (N = 243) % of patients	Control regimen (N = 241) % of patients	Odds ratio	95% CI	P value for odds ratio[a]
Complete response[b]					
0–120 h	72.0	60.6	1.80	1.21–2.66	0.003
0–24 h	87.7	79.3	2.10	1.25–3.52	0.005
>24–120 h	74.1	63.1	1.78	1.20–2.65	0.004
No vomiting					
0–120 h	76.5	62.2	2.14	1.43–3.22	≤0.001
0–24 h	88.9	80.5	2.17	1.27–3.69	0.004
>24–120 h	79.0	64.3	2.24	1.48–3.40	≤0.001
No use of rescue therapy					
0–120 h	82.3	79.7	1.23	0.78–1.96	0.373
0–24 h	94.2	92.9	1.32	0.63–2.77	0.468
>24–120 h	83.5	81.7	1.17	0.73–1.88	0.517
No significant nausea[c]					
0–120 h	73.1	69.7	1.24	0.83–1.87	0.290
0–24 h	92.1	89.5	1.45	0.77–2.76	0.254
>24–120 h	75.9	72.1	1.28	0.84–1.94	0.248

[a]P value of logistic model including terms for treatment, gender, use of concomitant emetogenic chemotherapy and geographic region.
[b]Complete response = no vomiting and no use of rescue therapy.
[c]For No significant nausea, the Ns varied from 237 to 242. No significant nausea = score of <25 mm on 100-mm visual analog scale.

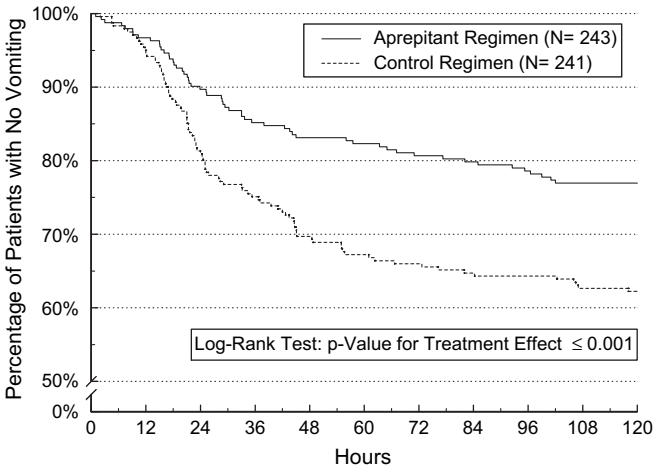

Figure 2. Percentage of patients with no vomiting over 120 h post-cisplatin (Kaplan–Meier curves for time to first vomiting episode from start of cisplatin treatment in the overall phase).

patient in the aprepitant group (patient took three tablets of ondansetron placebo instead of two) and upper gastrointestinal hemorrhage in one patient in the control group.

The two treatment groups had similar rates of laboratory and serious laboratory adverse events (Table 3). The rate of drug-related laboratory adverse events was somewhat higher in the aprepitant group (6.2% versus 2.0% control; P = 0.023). Serious laboratory adverse events occurred in four patients in the aprepitant group (one with decreased ionized calcium, one with increased blood creatinine, two with decreased platelet count) and in two patients in the control group (one with decreased blood sodium and one with decreased platelet count); none of these adverse events were considered drug-related. No patients discontinued due to laboratory adverse events.

discussion

Antiemetic treatment regimens that combine the NK_1 receptor antagonist aprepitant with a 5-HT_3 RA plus a corticosteroid on day 1, followed by aprepitant and dexamethasone on the subsequent days, have been shown to be superior to regimens that comprise only a 5-HT_3 RA plus a corticosteroid in providing complete response (no vomiting and no use of rescue therapy) in both the acute and delayed phases of vomiting in patients receiving cisplatin chemotherapy [11, 12]. These findings led to the recent recommendations for treating acute-phase vomiting with the triple-drug combination of aprepitant plus a 5-HT_3 RA and dexamethasone [16]. The current study was designed to compare the aprepitant regimen with a regimen similar to one frequently used in clinical practice, in which both the 5-HT_3 RA and corticosteroid are given for multiple days.

In this study, the aprepitant regimen was superior to the control regimen (ondansetron plus dexamethasone both given for 4 days) in providing complete response, primarily because of excellent efficacy in preventing vomiting. Complete response rates were higher in the aprepitant group for the overall phase (0–120 h post-cisplatin), as well as in separate assessments of the acute and delayed phases. As in previous studies, the between-group difference in the complete response rate was more pronounced in the delayed phase (11 percentage points) than in the acute phase (8 percentage points).

Acute-phase vomiting after cisplatin treatment is thought to be primarily mediated via the serotonin receptors, the site of action of 5-HT_3 RAs. The mechanism for post-cisplatin

Table 3. Summary of adverse events

	Aprepitant regimen ($N = 243$) *n* (%)	Control regimen ($N = 244$) *n* (%)
Clinical adverse events		
≥1 adverse event	192 (79.0)	199 (81.6)
Drug-related adverse events[a]	57 (23.5)	59 (24.2)
Serious adverse events	33 (13.6)	37 (15.2)
Serious drug-related adverse events[a]	2 (0.8)	1 (0.4)
Discontinued due to adverse events	0 (0)	4 (1.6)
Most common clinical adverse events		
Anorexia	34 (14.0)	36 (14.8)
Asthenia	33 (13.6)	37 (15.2)
Constipation	38 (15.6)	54 (22.1)
Diarrhea	31 (12.8)	23 (9.4)
Dyspepsia	33 (13.6)	27 (11.1)
Fatigue	22 (9.1)	15 (6.1)
Hiccups	24 (9.9)	24 (9.8)
Nausea	38 (15.6)	24 (9.8)
Vomiting	22 (9.1)	24 (9.8)
Most common serious adverse events		
Febrile neutropenia	1 (0.4)	3 (1.2)
Neutropenia	3 (1.2)	4 (1.6)
Diarrhea	3 (1.2)	1 (0.4)
Nausea[b]	3 (1.2)	3 (1.2)
Vomiting[b]	7 (2.9)	4 (1.6)
Pneumonia	4 (1.6)	2 (0.8)
Dehydration	5 (2.1)	3 (1.2)
Laboratory adverse events[c]		
≥1 adverse event	51 (21.1)	52 (21.3)
Drug-related adverse events[a]	15 (6.2)	5 (2.0)
Serious adverse events	4 (1.7)	2 (0.8)
Serious drug-related adverse events[a]	0 (0)	0 (0)
Discontinued due to adverse events	0 (0)	0 (0)

[a]Determined by the investigator to be possibly, probably or definitely related to study drug.

[b]During the diary period, nausea and vomiting were considered adverse events only if they resulted in hospitalization (i.e. serious adverse event). After the diary period, nausea and vomiting were captured as adverse events.

[c]Percent of total patients with one or more laboratory tests post-baseline.

delayed-phase vomiting is not well understood, but the generally lower efficacy of 5-HT_3 receptor antagonists in the delayed phase points to a lesser role for serotonin. Another supporting line of evidence for a non-serotonin mechanism comes from the finding that the urinary level of the serotonin metabolite 5-hydroxyindoleacetic acid, which reflects gastrointestinal serotonin release and turnover, increases in association with cisplatin-induced acute-phase vomiting, but returns to baseline levels during delayed-phase vomiting [17]. A recent analysis of the time course of the antiemetic effect of 5-HT_3 receptor antagonists and the NK_1 receptor antagonist aprepitant indicated that while serotonin-dependent mechanisms predominate in the acute phase, NK-1-dependent mechanisms predominate in delayed-phase vomiting [10].

Nausea occurred in fewer patients in the aprepitant group, but the results were not significantly different from those in the control group. This result is in line with other aprepitant studies in which patients received either highly [11] or moderately [18] emetogenic chemotherapy, which suggests that the neurokinin-1 receptor antagonists may have less impact on the nausea component of chemotherapy-induced nausea and vomiting. In general, the control of nausea lags behind the control of vomiting, perhaps because of the difficulty of measuring this subjective symptom and the possibility that patients confuse nausea with anorexia, fatigue or pyrosis [19].

Patients in the aprepitant group also had a longer duration of protection against the first vomiting episode: the Kaplan–Meier curves for time to first vomiting began to show a visual separation at 10 h and a *post hoc* analysis showed a statistically significant separation at 21 h. Similar findings were observed in other studies that compared an aprepitant regimen and various multiple-day ondansetron-based control regimens in patients receiving highly emetogenic chemotherapy [11, 12] and in breast cancer patients receiving moderately emetogenic chemotherapy [18].

In the current study, the adverse event profile was typical of a population of patients with cancer receiving high-dose cisplatin chemotherapy. The overall incidences and profiles of clinical and laboratory adverse experiences were similar between the treatment regimens. Although the incidence of drug-related laboratory adverse events was slightly higher in the aprepitant group, there was no clinically meaningful difference between groups in the incidence of any specific event. Previous large studies comparing an aprepitant regimen with an ondansetron-based control regimen had similar findings [11, 12, 18]. Whereas two previous studies showed trends for higher rates of asthenia/fatigue and hiccups in the aprepitant group than in the ondansetron-based control groups [11, 12], neither the current study nor the recent study conducted in patients receiving moderately emetogenic chemotherapy [18] showed an association of either of these adverse events with aprepitant. In the current study, the incidences of stomatitis, urinary tract infection and nausea as an adverse event (occurring after the 5-day diary period or resulting in hospitalization during the diary period) were slightly higher in the aprepitant group, but the findings were not considered clinically meaningful. Other studies have also shown similar or slightly higher rates of nausea as an adverse event with the aprepitant regimen compared with control [11, 12, 18].

conclusions

In patients receiving highly emetogenic chemotherapy, the aprepitant regimen was superior to a control regimen (ondansetron and dexamethasone both given for 4 days) in preventing chemotherapy-induced nausea and vomiting in the overall, acute and delayed phases. The comparative benefit of the aprepitant regimen was especially strong in providing protection against delayed-phase vomiting. These findings clearly establish the superior efficacy profile of the aprepitant regimen versus a multiple-day ondansetron + dexamethasone regimen for patients receiving highly emetogenic chemotherapy.

Thus, the aprepitant regimen should be considered a new standard of antiemetic therapy for cisplatin-treated patients.

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