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Randomized, Double-Blind, Phase III Study of Fosnetupitant Versus Fosaprepitant for Prevention of Highly Emetogenic Chemotherapy-Induced Nausea and Vomiting: CONSOLE

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abstract

PURPOSE We evaluated the efficacy and safety of fosnetupitant (FosNTP) versus fosaprepitant (FosAPR) for preventing highly emetogenic chemotherapy-induced nausea and vomiting. This phase III study was the first head-to-head comparison between two different neurokinin-1 receptor antagonists in combination with palonosetron and dexamethasone.

PATIENTS AND METHODS Patients scheduled to receive cisplatin-based chemotherapy were randomly assigned 1:1 to FosNTP 235 mg or FosAPR 150 mg in combination with palonosetron 0.75 mg and dexamethasone. The primary end point was overall (0-120 hours) complete response (CR; no emetic event and no rescue medication) rate, stratified by sex and age category, to show the noninferiority of FosNTP to FosAPR (noninferiority margin, –10% for the difference in the overall CR rate).

RESULTS Overall, 795 patients were randomly assigned, of whom 785 received the study drug (FosNTP [N = 392] *v* FosAPR [N = 393]) and were evaluated for efficacy and safety. The overall CR rate was 75.2% versus 71.0%, respectively (Mantel-Haenszel common risk difference, 4.1%; 95% CI, –2.1% to 10.3%), demonstrating noninferiority of FosNTP to FosAPR. The CR rates in the acute (0-24 hours), delayed (24-120 hours), and beyond delayed (120-168 hours) phases, and at 0-168 hours were 93.9% versus 92.6%, 76.8% versus 72.8%, 86.5% versus 81.4%, and 73.2% versus 66.9%, respectively. The incidence rates of treatment-related adverse events with FosNTP versus FosAPR were 22.2% versus 25.4%, whereas adverse events or treatment-related adverse events relevant to injection site reactions were 11.0% versus 20.6% ($P < .001$) and 0.3% versus 3.6% ($P < .001$), respectively.

CONCLUSION FosNTP demonstrated noninferiority to FosAPR, with a favorable safety profile and lower risk for injection site reactions. Thus, FosNTP is valuable in the prophylaxis of acute, delayed, and beyond delayed chemotherapy-induced nausea and vomiting.

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ASSOCIATED CONTENT

Data Supplement
Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

Chemotherapy-induced nausea and vomiting (CINV) are toxicities that develop frequently following chemotherapy for malignant tumors. In particular, CINV induced by cisplatin occurs mainly following chemotherapy over several days, and therefore, often occurs after discharge from the hospital, causing significant discomfort to the patient beyond the recognition of health care professionals.[1]

Antiemetic guidelines recommend proactive preventive measures when using anticancer drugs classified as highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy. For most patients receiving HEC and for some receiving moderately emetogenic chemotherapy, a triplet therapy comprising a neurokinin-1 (NK_1) receptor antagonist (RA), a serotonin ($5\text{-}HT_3$) RA, and dexamethasone (DEX) is considered as the basic therapy. Furthermore, some guidelines recommend a quartet therapy including olanzapine in addition to the above components.[2-5]

Fosaprepitant (FosAPR) is a widely used NK_1 RA, the injectable prodrug of aprepitant,[6] which can be administered to patients with difficulty in eating or drinking, thereby improving compliance compared with oral drugs. FosAPR has been reported to be associated with a high frequency of injection site reactions (ISRs) with cisplatin dosing, resulting in clinical concerns and suggesting an unmet medical need.[7-9]

CONTEXT

Key Objective

Does fosnetupitant (FosNTP) demonstrate noninferiority to fosaprepitant (FosAPR) with a lower incidence of injection site reactions for preventing chemotherapy-induced nausea and vomiting in patients receiving cisplatin-based highly emetogenic chemotherapy?

Knowledge Generated

The overall (0-120 hours; acute [0-24 hours] plus delayed [24-120 hours]) complete response rate for the primary end point was 75.2% with FosNTP versus 71.0% with FosAPR (Mantel-Haenszel common risk difference, 4.1%; 95% CI, –2.1% to 10.3%), demonstrating noninferiority of FosNTP to FosAPR. The complete response rates in the acute, delayed, and beyond delayed (120-168 hours) phases, and at 0-168 hours were 93.9% versus 92.6%, 76.8% versus 72.8%, 86.5% versus 81.4%, and 73.2% versus 66.9% with FosNTP versus FosAPR, respectively. The incidence of injection site reactions was significantly lower with FosNTP than with FosAPR.

Relevance

FosNTP is valuable in the prophylaxis of acute, delayed, and beyond delayed chemotherapy-induced nausea and vomiting.

Fosnetupitant (FosNTP) is an injectable phosphorylated prodrug of netupitant. Its active form, netupitant, is characterized by high selectivity and affinity to the NK_1 receptor and has a longer elimination half-life than that of aprepitant.[6,10] In the United States and European Union, a fixed-dose combination of FosNTP 235 mg and palonosetron (PALO; a 5-HT_3 RA) 0.25 mg (intravenous [IV] netupitant-palonosetron [NEPA]) has been approved for preventing CINV.[11,12]

In Japan, approaches have focused on the development of FosNTP as a single agent. A phase I study confirmed a good safety profile with up to 353 mg of FosNTP, with rapid conversion to its active form after administration in healthy adults (data on file). Furthermore, a clinical pharmacology study on drug interaction between FosNTP and granisetron, a 5-HT_3 RA, confirmed a good safety profile and the absence of drug interactions with concurrent use of granisetron (data on file).

A double-blind, randomized, phase II study in patients receiving cisplatin confirmed the superiority of FosNTP 235 mg to placebo in combination with PALO 0.75 mg and DEX in complete response (CR; no emetic event and no rescue medication) rate during the overall phase (0-120 hours after the start of cisplatin administration; acute [0-24 hours] plus delayed [24-120 hours]) and a satisfactory safety profile, with a very low frequency of ISRs.[10] This phase II study extended the efficacy observation period beyond 120 hours to 168 hours for the exploratory evaluation, suggesting a higher efficacy of FosNTP compared with placebo.

On the basis of these findings, FosNTP appears to be effective not only in acute and delayed CINV but also in beyond delayed CINV and has the potential to overcome the risk of developing ISRs with FosAPR administration. Hence, we conducted a randomized, phase III study to evaluate the efficacy and safety of FosNTP versus FosAPR as a control drug when combined with PALO and DEX (JapicCTI-194611).

PATIENTS AND METHODS

Study Design

This multicenter study was conducted at 82 study sites (Data Supplement, online only). The study comprised two parts—a single chemotherapy cycle (S-cycle; course 1) and multiple chemotherapy cycles (M-cycles; courses 2-4; Data Supplement). The S-cycle evaluated the noninferiority of FosNTP to FosAPR when administered once IV in combination with PALO 0.75 mg and DEX to patients receiving cisplatin-based chemotherapy. The M-cycles evaluated the safety of administering up to three courses of FosNTP to patients who had completed the S-cycle and agreed to participate in the M-cycles.

This study was conducted according to the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines and was conducted at all participating study sites after institutional review board approval.

Patients

The main inclusion criteria for the S-cycle were patients with malignant tumors who were age $\geq$ 20 years; had not received chemotherapy or had received prior chemotherapy classified as low or minimal emetic risk and were scheduled to receive chemotherapy including cisplatin $\geq$ 70 mg/m^2; had an Eastern Cooperative Oncology Group performance status score of 0-1; and had adequately maintained bone marrow, liver, and kidney functions. Patients who had emetic events or nausea within 7 days, had undergone surgery or received radiotherapy to the abdomen (below the

diaphragm) or pelvis within 7 days, and had received antiemetic drugs within 2 days before enrollment were excluded.

The M-cycles included patients who were scheduled to continue chemotherapy including cisplatin ≥ 70 mg/m^2.

Patients provided written consent for each part and were enrolled.

Random Assignment and Blinding

Eligible patients who agreed to participate in the study were enrolled by the investigators via an interactive web response system and were randomly assigned 1:1 to the FosNTP or FosAPR groups according to dynamic allocation per stratification factors (age category [≥ 55 years $v <$ 55 years], sex, and study site) in the S-cycle. Moreover, the S-cycle adopted a double-blind, double-dummy method. Since the study drug vials of FosNTP and FosAPR were distinguishable by appearance, unblinded pharmacists prepared the study drugs, PALO and DEX. The unblinded pharmacists were mandatorily required to maintain the blinding procedures.

The M-cycles were conducted in an uncontrolled and unblinded manner.

Study Treatments

During the S-cycle, in the FosNTP group, FosNTP 235 mg, PALO 0.75 mg, and DEX 9.9 mg were mixed and infused for 30 minutes, starting 1 hour before cisplatin administration on day 1. In the FosAPR group, FosAPR 150 mg was infused for 30 minutes, starting 1 hour before cisplatin administration, and PALO 0.75 mg and DEX 9.9 mg were separately infused for 30 minutes because of a potential risk of incompatibility of FosAPR with PALO,[13] starting 30 minutes before FosAPR administration or immediately following FosAPR administration by each study site. To maintain blinding, physiologic saline was administered in the FosNTP group when PALO and DEX were administered in the FosAPR group. On days 2-4, DEX 6.6 mg was administered IV in both groups.

Similarly, in the M-cycles, FosNTP, PALO, and DEX were mixed and infused for 30 minutes, starting 1 hour before cisplatin administration (up to three courses) on day 1. On days 2-4, DEX was administered IV (6.6 mg) or orally (8 mg).

The study drugs were administered through peripheral veins in each cycle.

Assessments

Emetic events and nausea were recorded in a patient diary every 24 hours until 168 hours in each course. For assessing the number of emetic events that occurred, one episode was counted as one occurrence. Nausea was assessed on a 4-point Likert scale (none, mild, moderate, or severe). Rescue medication was administered up to 168 hours after cisplatin administration if the investigator judged it necessary. Administration of rescue medication for nausea was considered when the nausea was severe (with inability to eat and drink). The assessments of efficacy (0-168 hours) in the S-cycle were performed under hospitalization.

Adverse events (AEs) were graded according to the Common Terminology Criteria for Adverse Events version 5.0, and their causal relationships with the study drugs were assessed by the investigator on a 5-point scale (definite, probably related, possibly related, unlikely related, or not related). Events assessed as definite, probably related, or possibly related were considered as treatment-related AEs (TRAEs). Emetic events and nausea occurring at 0-168 hours after the start of cisplatin administration were not regarded as AEs as they were indices for efficacy evaluation. However, emetic events and nausea that continued or newly occurred beyond 168 hours were regarded as AEs. AEs, including ISRs, were assessed after the start of study drug administration.

End Points

In the S-cycle, the primary end point was the overall (0-120 hours after the start of cisplatin administration) CR (no emetic event and no rescue medication) rate. The main secondary end points were the CR rate (except for the overall phase); complete protection (CR plus no more than mild nausea) rate; total control (CR plus no nausea) rate; no emetic events; no nausea; no significant (no more than mild) nausea during the acute (0-24 hours), delayed (24-120 hours), and overall phases and at 0-168 hours and 120-168 hours; and safety, including ISRs.

The primary end point in the M-cycles was safety. ISRs and efficacy were assessed as secondary end points.

Statistical Analysis

For the primary analysis of the primary end point in the S-cycle, differences in the overall CR rate were analyzed by comparing the CR rate of FosNTP with that of FosAPR stratified by age category and sex and calculated on the basis of the Mantel-Haenszel method in the full analysis set (FAS; among patients who received the study drugs, those who received PALO, DEX, and cisplatin on day 1). A 2-sided 95% CI was also calculated using Newcombe's method.[14] If the lower confidence bound was higher than –10% (noninferiority margin), noninferiority was considered to be confirmed, and if it was higher than 0%, superiority was also considered to be confirmed. Regarding the imputation of missing data, the criteria for CR were considered as not met at the time point where the data were missing.

The overall CR rate was assumed to be 76.8% in both groups on the basis of the results from a phase II study.[10] The number of patients needed when the noninferiority margin was 10%, the 1-sided significance level was 2.5%, and the statistical power was 90% was calculated. Therefore, considering that approximately 5% of the enrolled patients would be excluded from the FAS, the target number of patients was set at 790. In the M-cycles, 120 patients

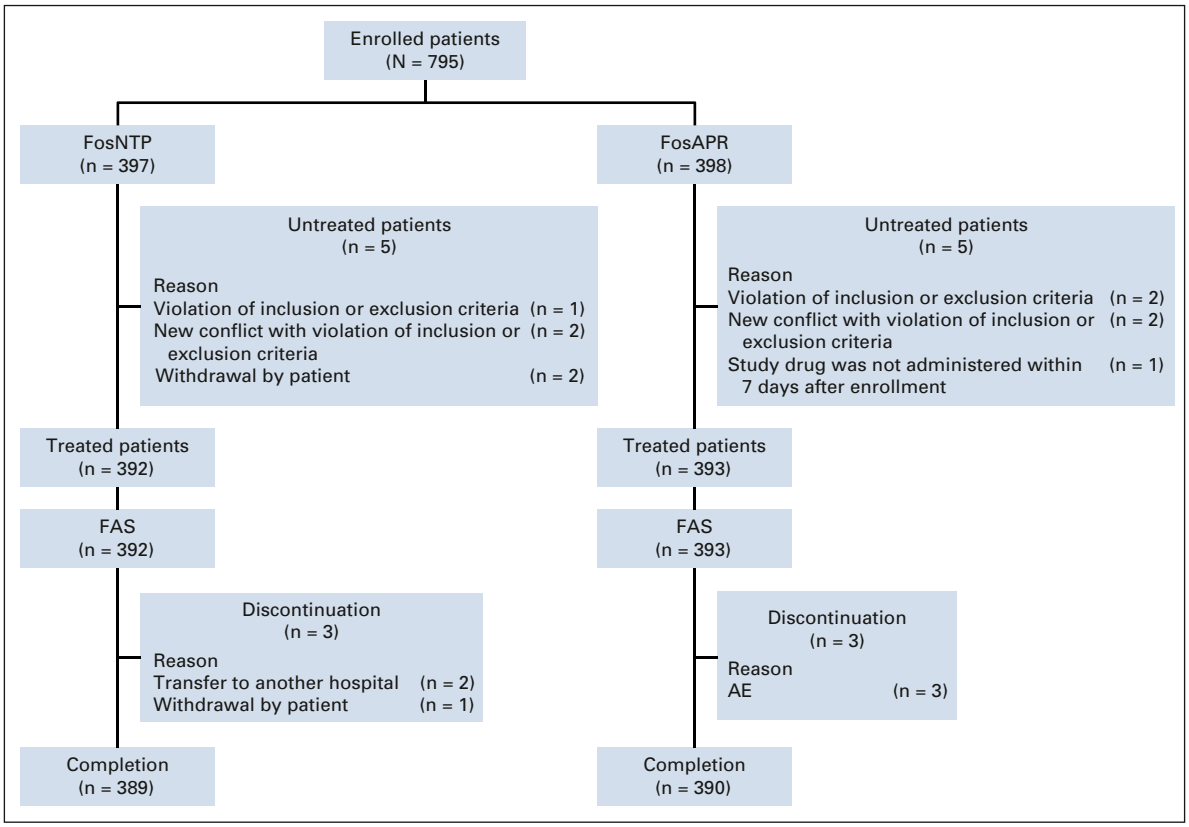

FIG 1. CONSORT diagram (S-cycle). A total of 795 patients were enrolled in the S-cycle. The study drug was administered to 785 patients (FosNTP *v* FosAPR, n = 392 *v* n = 393, respectively), and all of them were evaluated for efficacy and safety. AE, adverse event; FAS, full analysis set; FosAPR, fosaprepitant; FosNTP, fosnetupitant; S-cycle, single chemotherapy cycle.

randomly assigned in the S-cycle were planned to be enrolled for evaluating safety and efficacy.

For analyzing the secondary end points, the CR rate; complete protection rate; total control rate; and rates of no nausea, no significant nausea, and no emetic events in the FAS were calculated, and their 95% CIs were estimated. For the safety analysis, patients who received the study drugs were analyzed. The time to treatment failure (TTF; time to first emetic event or use of rescue medication) curve was estimated using the Kaplan-Meier method. As a post hoc analysis, TTF was analyzed using a log-rank test, with hazard ratio and 95% CI, and the incidence of CINV was analyzed every 24 hours until 168 hours. The incidence rate of ISRs and 95% CIs were calculated, and Fisher's exact test was performed.

Statistical analyses were performed using SAS statistical software (version 9.4; SAS Institute Inc, Cary, NC).

RESULTS

Patients

From February 2019 to March 2020, 795 patients were randomly assigned in the S-cycle, of whom 785 received the study drugs (FosNTP or FosAPR) and 779 completed the S-cycle (Fig 1). None of the patients who received the study drugs were excluded from the FAS. The patient background characteristics of the FAS were generally balanced between the two groups (Table 1). Most of the enrolled patients were men and had lung cancer.

Chemotherapy regimens used and the presence or absence of radiotherapy during the study period are listed in the Data Supplement. Approximately half of the regimens used in combination with cisplatin (including radiotherapy) comprised cisplatin plus vinorelbine in both groups. A similar number of patients received concurrent radiotherapy (excluding irradiation of the abdomen or pelvis) in both groups.

The proportion of patients who received rescue medication during the efficacy observation period was 16.3% versus 17.8% with FosNTP versus FosAPR, respectively.

Efficacy

In the S-cycle, the overall CR rate (the primary end point) was 75.2% versus 71.0% with FosNTP versus FosAPR, respectively. The intergroup difference in the overall CR rate was 4.1% (95% CI, –2.1% to 10.3%), which demonstrated the noninferiority of FosNTP to FosAPR. The superiority, however, was not demonstrated.

CR rates by phase are illustrated in Figure 2, and the results of other efficacy assessments are presented in the Data

TABLE 1. Patient Characteristics (S-cycle)

Characteristic	FosNTP (n = 392)	FosAPR (n = 393)
Age, years		
Median (range)	67.0 (40-81)	66.0 (33-82)
< 55, No. (%)	50 (12.8)	50 (12.7)
≥ 55, No. (%)	342 (87.2)	343 (87.3)
Sex, No. (%)		
Male	301 (76.8)	302 (76.8)
Female	91 (23.2)	91 (23.2)
Drinking history, No. (%)		
No	141 (36.0)	128 (32.6)
Rarely (once per month)	40 (10.2)	41 (10.4)
Occasionally (once per week)	37 (9.4)	43 (10.9)
Regularly (once per day)	174 (44.4)	181 (46.1)
Smoking history, No. (%)		
Nonsmoker	62 (15.8)	72 (18.3)
Stopped smoking 180 days before registration	167 (42.6)	166 (42.2)
Stopped smoking within 180 days before registration	136 (34.7)	128 (32.6)
Smoker	27 (6.9)	27 (6.9)
Motion sickness, No. (%)		
No	357 (91.1)	360 (91.6)
Yes	35 (8.9)	33 (8.4)
Malignant tumor, No. (%)		
Lung	353 (90.1)	341 (86.8)
Esophagus	21 (5.4)	24 (6.1)
Head and neck	7 (1.8)	10 (2.5)
Other	11 (2.8)	18 (4.6)
Dose of cisplatin, mg/m^2, No. (%)		
≥ 70 to < 80	144 (36.7)	165 (42.0)
≥ 80 to < 90	243 (62.0)	221 (56.2)
≥ 90	5 (1.3)	7 (1.8)

Abbreviations: FosAPR, fosaprepitant; FosNTP, fosnetupitant; S-cycle, single chemotherapy cycle.

Supplement. The CR rates in the delayed and beyond delayed (120-168 hours) phases and at 0-168 hours were 76.8% versus 72.8%, 86.5% versus 81.4%, and 73.2% versus 66.9%, respectively. The hazard ratio for TTF was 0.789 (95% CI, 0.610 to 1.021; $P = .071$; Fig 3). The incidence of CINV and overall CR rates in the subgroup are shown in Figure 4 and the Data Supplement.

Safety

In the S-cycle, an intergroup similarity was observed in the proportions of patients who developed AEs, TRAEs, and TRAEs of grade ≥ 3 (99.5% *v* 99.0%, 22.2% *v* 25.4%, and 2.6% *v* 3.1% with FosNTP *v* FosAPR, respectively; Data Supplement). The proportion of patients who developed TRAEs of grade ≥ 3 was 1.0% or less in both groups. TRAEs that were observed in ≥ 5% of patients in either group (FosNTP *v* FosAPR) were constipation (11.2% *v* 13.7%, respectively) and hiccups (4.8% *v* 7.1%, respectively).

The proportions of patients who developed AEs or TRAEs relevant to ISRs were significantly lower with FosNTP versus FosAPR—11.0% versus 20.6% ($P < .001$) and 0.3% versus 3.6% ($P < .001$), respectively (Table 2).

No serious TRAEs and AEs leading to death were observed in the FosNTP group (Data Supplement). The serious TRAEs that developed in the FosAPR group were ischemic colitis and erythema multiforme.

Multiple Chemotherapy Cycles

A total of 129 patients were enrolled, of whom 126 (S-cycle: FosNTP [n = 65]; FosAPR [n = 61]) were treated (Data Supplement). AEs that occurred in the M-cycles are summarized in the Data Supplement. The proportions of patients who developed AEs and TRAEs were similar among different courses and were also approximately the same as those in the S-cycle. The only TRAE observed in ≥ 5% of patients was hiccups (5.9% in course 3). The only TRAE relevant to ISR developed in one patient (1.2%) during course 4. Efficacy results by phase are shown in the Data Supplement. The overall CR rate was approximately the same as that in the S-cycle, and efficacy was maintained without attenuation.

DISCUSSION

To the best of our knowledge, this was the first randomized, double-blind, controlled, phase III head-to-head comparison of the inhibitory effect of different NK_1 RAs on CINV when used in combination with PALO 0.75 mg and DEX in patients receiving HEC.

This study demonstrated the noninferiority of FosNTP to FosAPR in the overall CR rate, which was the primary end point. In clinical studies of CINV that have been reported so far, the assessment periods for CINV were set at 120 hours. Recently, however, an observational study of CINV investigated the occurrence of nausea or vomiting beyond 120 hours.[15] The study reported the presence of a certain number of patients who developed CINV after 120 hours, suggesting the importance of monitoring for beyond delayed CINV that develops after 120 hours. In our study, the efficacy assessment was continued until 168 hours, indicating that all efficacy parameters tended to be higher with FosNTP than with FosAPR in the delayed and overall phases and in the observational period including 168 hours. Conceivably, the main reason for this is a possible contribution of differences in the pharmacokinetic profiles of the two drugs—difference in elimination half-life in plasma of the active form.[6,10]

In the phase III study of IV NEPA in patients receiving HEC (approximately 96% of patients were treated with cisplatin),[16] the overall CR rate was 76.8% for the IV NEPA group, which was comparable with the results of our study (75.2%). One of

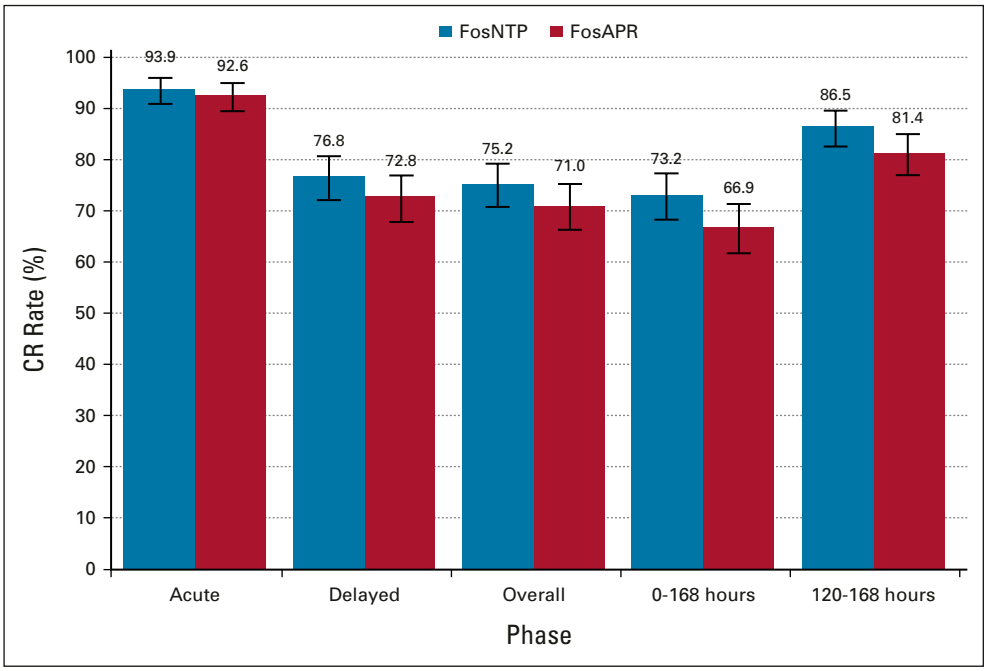

FIG 2. CR rate by phase (S-cycle). The CR (no emetic event and no rescue medication) rates during the acute (0-24 hours), delayed (24-120 hours), and overall (0-120 hours) phases and at 0-168 hours and 120-168 hours in the full analysis set were calculated and their 95% CIs were estimated. The overall CR rate was stratified by sex and age category. CR, complete response; FosAPR, fosaprepitant; FosNTP, fosnetupitant; S-cycle, single chemotherapy cycle.

the major differences between the two studies was the dosage of concomitant PALO (0.25 mg *v* 0.75 mg). A systematic review has reported no statistically significant difference in efficacy between the two PALO doses.[17] The efficacy results of our study were therefore considered to be robust.

This study showed that the safety profile of FosNTP was favorable and the observed TRAEs were events that have already been reported for NK_1 RAs[18,19] and were manageable. Except for the ISRs, the safety profiles of FosNTP and FosAPR were similar. The proportion of patients who developed AEs and TRAEs relevant to ISRs was significantly lower with FosNTP than with FosAPR. The proportion of patients who developed TRAEs relevant to ISRs in this study (0.3%) was similar to that reported in a phase II study of FosNTP

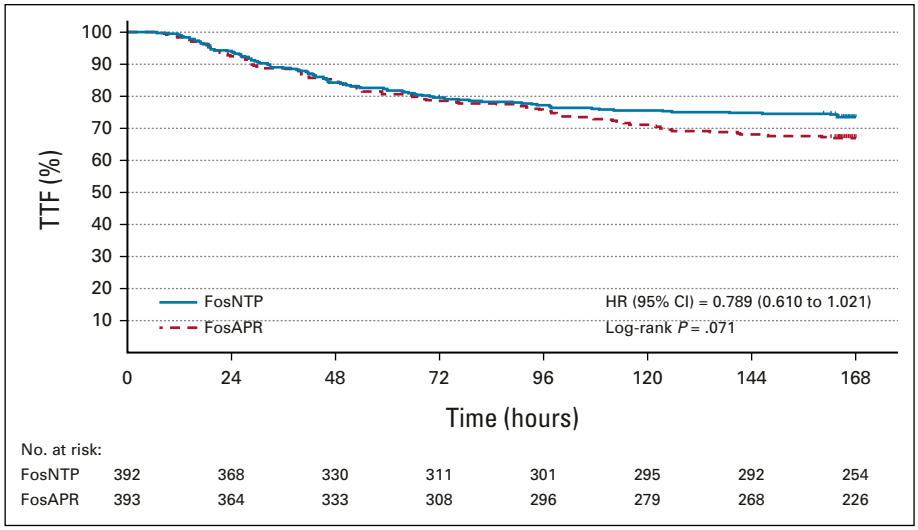

FIG 3. TTF (S-cycle). The TTF (time to first emetic event or use of rescue medication) curve was estimated using the Kaplan-Meier method. FosAPR, fosaprepitant; FosNTP, fosnetupitant; HR, hazard ratio; S-cycle, single chemotherapy cycle; TTF, time to treatment failure.

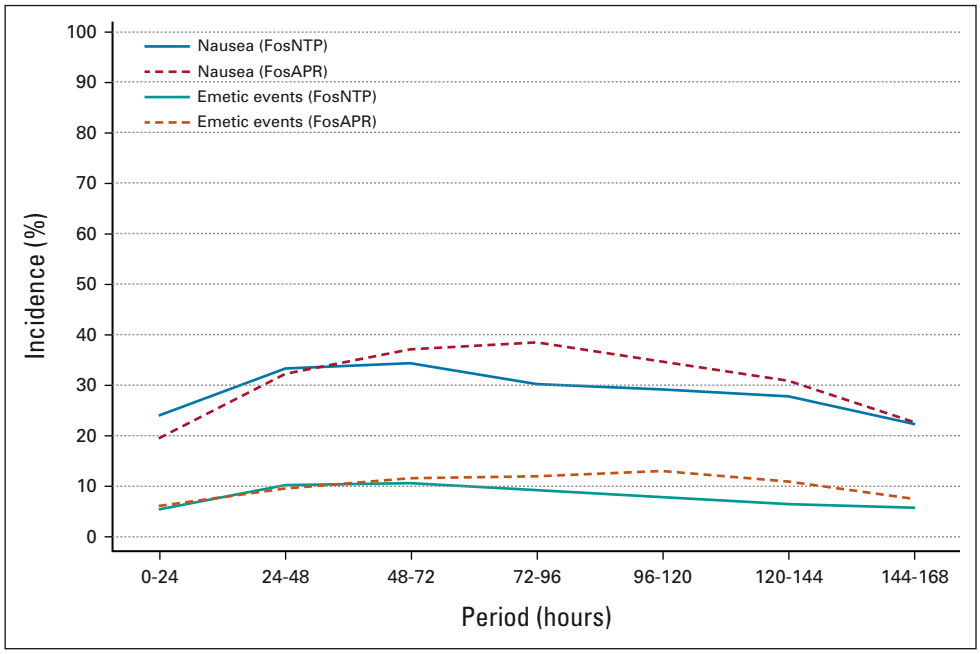

FIG 4. CINV incidence (S-cycle). CINV incidence (nausea and emetic events) was analyzed every 24 hours from the start of cisplatin administration to 168 hours. CINV, chemotherapy-induced nausea and vomiting; FosAPR, fosaprepitant; FosNTP, fosnetupitant; S-cycle, single chemotherapy cycle.

(1.0%)[10] and in the IV NEPA phase III study (0%)[16] in patients receiving cisplatin. Moreover, in a phase III safety study of FosNTP[20] and IV NEPA[21] conducted in patients receiving doxorubicin-cyclophosphamide or epirubicin-cyclophosphamide and who were known to have a higher risk of ISRs with FosAPR,[8,9,22-26] no TRAEs relevant to ISRs were observed. These data suggested that the risk of developing ISRs caused by FosNTP is very low. Moreover, FosNTP showed a good safety profile with no increase in events relevant to ISRs in patients receiving FosNTP over multiple cycles.

Our study implemented simultaneous administration of FosNTP with PALO and DEX in one infusion bag without an incompatibility risk, which enabled shortening the total infusion time versus sequential dosing of FosAPR and PALO with DEX.[13] Thus, the ability to mix coadministered agents in a single IV bag is considered to be advantageous in a clinical setting. Recently, such dosing convenience was also found in the Ottoboni et al[27] trial, although it was not designed to evaluate the admixture of aprepitant injectable emulsion with PALO and DEX.

TABLE 2. Summary of ISRs (S-cycle)

	AEs, No. (%)			TRAEs, No. (%)		
Preferred Term	**FosNTP (n = 392)**	**FosAPR (n = 393)**	***P*[a]**	**FosNTP (n = 392)**	**FosAPR (n = 393)**	***P*[a]**
Total ISRs	43 (11.0)	81 (20.6)	< .001	1 (0.3)	14 (3.6)	< .001
Injection site pain	22 (5.6)	52 (13.2)	< .001	1 (0.3)	11 (2.8)	.006
Injection site erythema	10 (2.6)	19 (4.8)	.129	0 (0.0)	3 (0.8)	.249
Injection site induration	4 (1.0)	11 (2.8)	.115	0 (0.0)	2 (0.5)	.499
Injection site swelling	6 (1.5)	5 (1.3)	.773	0 (0.0)	0 (0.0)	—
Injection site vasculitis	5 (1.3)	5 (1.3)	1	0 (0.0)	1 (0.3)	1
Infusion site pain	0 (0.0)	2 (0.5)	.499	0 (0.0)	0 (0.0)	—
Injection site phlebitis	2 (0.5)	1 (0.3)	.624	0 (0.0)	0 (0.0)	—
Injection site thrombosis	1 (0.3)	1 (0.3)	1	0 (0.0)	0 (0.0)	—
Infusion site phlebitis	0 (0.0)	1 (0.3)	1	0 (0.0)	0 (0.0)	—

Abbreviations: AE, adverse event; FosAPR, fosaprepitant; FosNTP, fosnetupitant; ISR, injection site reaction; S-cycle, single chemotherapy cycle; TRAE, treatment-related adverse event

[a]Fisher's exact test.

The ASCO and National Comprehensive Cancer Network guidelines recommend a quartet therapy.[2,3] In the Japanese guidelines,[5] however, a triplet therapy is recommended for patients receiving HEC, and a quartet therapy including olanzapine is carefully administered in appropriate patients. A limitation of this study was the lack of comparison with a quartet therapy including olanzapine.

In conclusion, the noninferiority of FosNTP to FosAPR was demonstrated in the overall CR rate in patients receiving HEC in combination with PALO and DEX. The proportion of patients who developed ISRs was significantly lower with FosNTP than with FosAPR, confirming the good safety profile of FosNTP. FosNTP is valuable in the prophylaxis of acute, delayed, and beyond delayed CINV.

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PRIOR PRESENTATION

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CLINICAL TRIAL INFORMATION

A phase III, randomized, double-blind, multicenter, active control study of Pro-NETU for the prevention of chemotherapy induced nausea and vomiting (CINV) in patients receiving cisplatin-based highly emetogenic chemotherapy (HEC) (JapicCTI-194611); CONSOLE.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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DATA SHARING STATEMENT

The sponsor's policy on data sharing may be found at https://www.taiho.co.jp/en/science/policy/clinical_trial_information_disclosure_policy/index.html.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Randomized, Double-Blind, Phase III Study of Fosnetupitant Versus Fosaprepitant for Prevention of Highly Emetogenic Chemotherapy-Induced Nausea and Vomiting: CONSOLE

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