**Background**

- Fosnetupitant (FosNTP) is a novel neurokinin 1 receptor antagonist (NK1RA) with favorable antiemetic efficacy in patients receiving cisplatin-based chemotherapy.
- In two studies that evaluated Fosnetupitant in patients receiving cisplatin-based chemotherapy, chemotherapy-induced nausea and vomiting (CINV) events were evaluated for up to 168 hours after cisplatin administration. [1-3]
- Fosnetupitant showed a tendency toward improving CINV control at 0-168 hours in previous studies, however, its antiemetic efficacy in this prolonged phase needs further evaluation.
- Patient-related risk factors described in various guidelines include young age, female sex, and drinking history (4, 5), although CINV risk factors for cisplatin-based chemotherapy at 0-168 hours have not been clearly extracted.
- This study assessed the efficacy of Fosnetupitant in combination with palonosetron and dexamethasone, and identified risk factors for CINV for up to 168 hours after treatment using pooled data from Japanese studies.

**Methods**

- A pooled analysis of randomized phases III and II/II/II studies was performed to compare the efficacy of Fosnetupitant and fosaprepitant (FosAPR) in patients receiving cisplatin-based chemotherapy.
- In this analysis, the overall population was defined as all patients in the FosNTP 81 mg, FosNTP 235 mg, FosAPR, and placebo groups. The population combining the FosNTP 235 mg and FosAPR groups comprised the NK1RA evaluable population.
- Observation period were acute (0-24 hours), delayed (24-120 hours), overall (0-120 hours), extended overall (0-168 hours), extended delayed (24-168 hours), and beyond delayed (120-168 hours), respectively.

**Efficacy of FosNTP**

- The primary endpoint of both studies was the overall complete response (CR); no emetic event and no rescue medication use.
- The CR, total control (TC), and no nausea rates in each phase were calculated in each population and each study, and the differences in treatment outcomes between the FosNTP 235 mg and FosAPR groups were determined. Their rate difference and 95% confidence intervals (CIs) were also calculated. The two groups were compared using Fisher’s exact test.

**Exploring CINV risk factors**

- Risk factors for CINV were explored from the following patient background factors in advance for analysis: age (≤55 years/55 years), sex (male/female), Eastern Cooperative Oncology Group performance status (0/1), drinking history (no or rarely), smoking history (no), motion sickness (yes/no), pregnancy-associated vomiting (yes/no), type of cancer (lung/other), cisplatin dose (≤80 mg/m2/≥80 mg/m2), NK1RA (FosNTP 81 mg/FosNTP 235 mg/FosAPR/placebo), and treatment failure in 0-120 hours (no/yes).
- Univariate and multivariate logistic regression were performed for the overall and NK1RA evaluable population with treatment failure (no CR) in each phase as a response variable and the aforementioned patient background factors as explanatory variables. The odds ratio, 95% CI, and p-value for each background factor were calculated.
- Background factors significant at p < 0.05 using the backward stepwise procedure were identified as risk factors.
- The Cochran-Armitage trend test was performed to evaluate the association between the number of risk factors identified and treatment failure.
- The time to treatment failure (TTF, time to the first emetic event or the use of rescue medication) was estimated according to the number of risk factors using the Kaplan-Meier method.

**Table 1. Risk differences for complete response, no nausea, and total control in the FosNTP 235 mg and FosAPR groups (NK1RA evaluable population: n=980)**

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Complete response (%)</th>
<th>No nausea (%)</th>
<th>Total control (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FosNTP 235 mg</td>
<td>358</td>
<td>45.7</td>
<td>58.0</td>
<td>73.4</td>
</tr>
<tr>
<td>FosAPR</td>
<td>330</td>
<td>48.2</td>
<td>59.1</td>
<td>74.3</td>
</tr>
</tbody>
</table>

**Results**

**Efficacy of FosNTP: summary**

- The CR rate at 0-168 h was significantly better in the FosNTP 235 mg than in the FosAPR group (rate difference = 6.8%, 95% CI = 1.0-12.7, p = 0.022) in the combined cohort of NK1RA evaluable populations (n=980) (Table 1).

**Exploring CINV risk factors up to 168 hours: summary**

- The CINV risk factors at 0-168 hours were sex (female), performance status 1, drinking history (no or rarely), smoking history (no), and NK1RA (placebo).
- The CINV risk factor during the beyond delayed phase was treatment failure at 0-120 hours (yes).
- TTF tended to deteriorate as the number of risk factors increased (Fig. 1).

**Exploring CINV risk factors up to 120 hours**

- The CINV risk factors during the overall phase were sex (female), performance status 1, drinking history (no or rarely), smoking history (no), motion sickness (yes), and NK1RA (placebo).

**Conclusion**

- This analysis revealed that Fosnetupitant had significantly greater antiemetic potency than FosAPR and indicated the importance of antiemetic therapy for up to 168 hours after cisplatin based chemotherapy including consideration of CINV risk factors.

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- The authors declare no financial conflict of interest.

**References**


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**Disclosure**

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**POOLED ANALYSIS OF FOSNETUPITANT-EVALUATED STUDIES AND RISK FACTORS FOR CISPLATIN-INDUCED NAUSEA AND VOMITING DURING THE EXTENDED OVERALL PHASE**

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