# DANGER-emesis

## SAFETY AND ANTIEMETIC EFFICACY OF WEEKLY ADMINISTRATION OF NETUPITANT/PALONOSETRON PLUS DEXAMETHASONE DURING FIVE WEEKS OF CONCOMITANT CHEMO-RADIATION

Abstract #ANTIE-002 – MASCC/AFSOS/ISOO Annual Meeting 2024

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## Introduction

- NEPA (netupitant 300 mg/palonosetron 0.5 mg) has not been evaluated for safety and efficacy as weekly antiemetic prophylaxis during concomitant radiotherapy and weekly cisplatin.
- Weekly NEPA per orally (p.o.) administration would reduce tablet intake compared to a 3-day aprepitant (p.o.) regimen.
- Safety has to be ruled out for potential accumulation and toxicity due to netupitant's longer half-life (~88 h) compared to aprepitant (9-13 h).

## Objectives

- Co-primary: Safety of weekly NEPA and dexamethasone (DEX).
- Co-primary: Proportion of subjects with sustained no emesis.

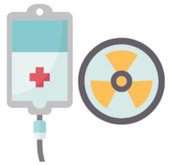
- Efficacy outcomes compared with a comparable cohort* using weekly fosaprepitant, palonosetron and dexamethasone:
  - Complete response day 1-5 and 1-35
  - No vomiting day 1-5 and 1-35
  - No significant nausea day 1-5 and day 1-35
  - No Nausea day 1-5 and day 1-35
  - Time to first emetic episode.

** GAND emesis, PMID: 26952945*

## Methods

- Single arm, phase II study (NCT03668639)

Patients with cervical cancer



Fractionated radiotherapy + concomitant weekly cisplatin 40 mg/m$^2$ for five weeks

Weekly NEPA p.o. (300 mg/0.5 mg) and DEX p.o. day 1-4 *(day 1: 12 mg, day 2-3: 8 mg, day 4: 4 mg)*

Weekly physician assessed AE registration and daily Patient Diary reporting nausea, vomiting and use of rescue medication

## Results

- Of 154 patients screened for inclusion, 73 patients were enrolled in the study, and 37 patients completed all five cycles of study treatment.

### Safety of weekly NEPA and DEX

| | Baseline n = 73 | Cycle 1 n = 73 | Cycle 2 n = 66 | Cycle 3 n = 59 | Cycle 4 n = 52 | Cycle 5 n = 37 | Total n = 73 |
|---|---|---|---|---|---|---|---|
| ≥ 1 AE | 55 (75%) | 72 (99%) | 65 (98%) | 59 (100%) | 48 (92%) | 32 (86%) | 73 (100%) |
| ≥ 1 AE grade 3 | 4 (5%) | 3 (4%) | 7 (11%) | 7 (12%) | 8 (15%) | 9 (24%) | 24 (33%) |
| ≥ 1 AE grade 4 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (3%) | 1 (1%) |
| ≥ 1 SAE | 1 (1%) | 0 (0%) | 3 (5%) | 1 (2%) | 1 (2%) | 2 (5%) | 5 (7%) |
| ≥ 1 TRAE | 0 (0%) | 61 (84%) | 54 (82%) | 51 (86%) | 40 (77%) | 24 (65%) | 69 (95%) |
| ≥ 1 TRAE grade 3 | 0 (0%) | 1 (1%) | 5 (8%) | 4 (7%) | 3 (6%) | 2 (5%) | 7 (10%) |
| ≥ 1 TRAE grade 4 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| ≥ 1 TRSAE | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |

*Table 1. Overview of Adverse Events (AEs), Serious Adverse Events (SAEs), Treatment-related AEs (TRAEs) and Treatment-related Serious Adverse Events (TRSAEs).*

**Definitions of treatment-related AEs (TRAEs)**
Relation to NEPA deemed as: *definitely related*, *probably related*, *possibly related*, or marked as missing.

Two TRAEs led to discontinuation of the study:

- Fatigue grade 2; urticaria grade 2

Seven patients experienced TRAEs grade 3:

- 1 abdominal distension; 2 fatigue; 1 flushing; 1 increased liver transaminase; 2 insomnia

## Conclusion

- NEPA plus DEX was safe and well-tolerated during weekly administration.
- NEPA plus DEX was highly effective as antiemetic prophylaxis.
- NEPA should be recommended as an option for weekly administration during concomitant radiotherapy and weekly cisplatin.

### Antiemetic efficacy of weekly NEPA and DEX

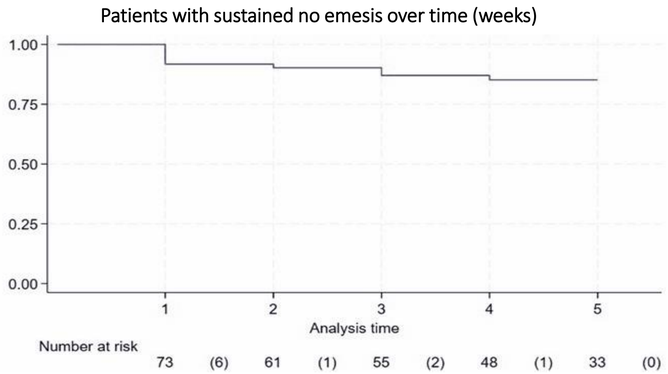



*Figure 1. Kaplan-Meier survival plot illustrating the incidence of patients with sustained no emesis over time (weeks).*

| | DANGER-emesis n = 73 | GAND-emesis, fosaprepitant cohort n = 118 | P value |
|---|---|---|---|
| Complete response | | | |
| Day 1-5 | 56 (77%) | 85 (72%) | 0.517 |
| Day 1-35 | 38 (52%) | 28 (24%) | 0.000 |
| No vomiting | | | |
| Day 1-5 | 68 (93%) | 107 (91%) | 0.795 |
| Day 1-35 | 63 (86%) | 91 (77%) | 0.144 |
| No significant nausea | | | |
| Day 1-5 | 63 (86%) | 95 (81%) | 0.449 |
| Day 1-35 | 45 (62%) | 31 (26%) | 0.000 |
| No nausea | | | |
| Day 1-5 | 36 (49%) | 55 (47%) | 0.887 |
| Day 1-35 | 13 (18%) | 18 (15%) | 0.704 |
| Mean time to first emetic episode (days) | 9.00 (SD 9.30) | 11.25 (SD 9.00) | 0.099 |

*Table 2. Efficacy outcomes compared with the fosaprepitant cohort from the GAND emesis study using the ITT population.*

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