# Clinical trial results:
# A phase 3, multicenter, randomized, double-blind, active control study to evaluate the safety and efficacy of IV pro-netupitant/palonosetron (260 mg/0.25 mg) combination for the prevention of chemotherapy-induced nausea and vomiting in repeated chemotherapy cycles in patients receiving highly emetogenic chemotherapy

## Summary

| | |
|---|---|
| EudraCT number | 2015-001800-74 |
| Trial protocol | AT DE CZ ES PL HR |
| Global end of trial date | 02 August 2016 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 December 2017 |
| First version publication date | 02 December 2017 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | NEPA-15-18 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02517021 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Helsinn Healthcare SA |
| Sponsor organisation address | Via Pian Scairolo 9, Lugano, Switzerland, 6912 |
| Public contact | Clinical Operation, Helsinn Healthcare SA, +41 91 985 21 21, daniel.voisin@helsinn.com |
| Scientific contact | Clinical Operation, Helsinn Healthcare SA, +41 91 985 21 21, daniel.voisin@helsinn.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 02 August 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 August 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 August 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to assess the safety and tolerability of a single dose of intravenous fosnetupitant/palonosetron (260 mg/0.25 mg) fixed-dose combination (IV NEPA FDC) infused over 30 minutes (min), with Oral dexamethasone, in initial and repeated cycles of highly emetogenic chemotherapy (HEC).

Protection of trial subjects:

This study was in compliance with the ethical principles founded in the Declaration of Helsinki, the International Conference on Harmonisation (ICH) guidelines regarding Good Clinical Practices and the European Union Directives on Clinical Trials. The appropriateness of the clinical trial protocol as well as the risks and benefits to study participants were approved by the relevant IECs/IRBs.
In addition, an independent Data Safety Monitoring Board (DSMB) was convened for the evaluation of safety data during the study in order to perform a qualitative safety assessment.

Background therapy:

Oral dexamethasone

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 17 November 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Israel: 2 |
| Country: Number of subjects enrolled | Italy: 18 |
| Country: Number of subjects enrolled | Serbia: 55 |
| Country: Number of subjects enrolled | Ukraine: 162 |
| Country: Number of subjects enrolled | United States: 12 |
| Country: Number of subjects enrolled | Poland: 113 |
| Country: Number of subjects enrolled | Spain: 8 |
| Country: Number of subjects enrolled | Croatia: 23 |
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | Czech Republic: 6 |
| Country: Number of subjects enrolled | Germany: 5 |
| Worldwide total number of subjects | 405 |
| EEA total number of subjects | 174 |

Notes:

| Subjects enrolled per age group | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 262 |
| From 65 to 84 years | 143 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Adult chemotherapy-naïve (at study entry) male or female patients with a diagnosis of malignant solid tumor requiring treatment with one of the reference HEC regimens on Day 1 of each cycle. Patients were enrolled in 56 study centers in 11 countries.

### Pre-assignment

Screening details:

A total of 400 patients (200 per treatment group) were planned to be randomized in the study. A total of 405 patients who met the inclusion criteria were eventually randomized. Of the 405 patients randomized, only one randomized patient in the Oral NEPA FDC group did not receive active study drug and reference HEC and was excluded from all analysis

### Period 1

| | |
|---|---|
| Period 1 title | Overall Trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Monitor, Data analyst, Carer, Assessor, Subject, Investigator |

Blinding implementation details:

The blinding of the study drugs was guaranteed by the use of identical placebos to the respective active drugs (double-dummy technique). When Oral NEPA FDC capsule was administered to subjects of the control group, a placebo capsule was administered to subjects of the test group. When IV NEPA FDC infusion was administered to subjects of the test group, an IV infusion of placebo was administered to subjects of the control group.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | IV NEPA FDC |

Arm description:

IV fosnetupitant/palonosetron (260 mg/0.25 mg) FDC (IV NEPA FDC) was to be administered as a 30-min infusion of a 50-mL solution on Day 1 of each cycle. The 30-min (±5 min) IV NEPA FDC infusion was to be started 30 min prior to the start of the reference chemotherapy administration. The 30-min IV infusion was to be completed before starting chemotherapy administration.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IV fosnetupitant/palonosetron fixed-dose combination for infusion (IV NEPA FDC) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of 30 min duration to begin 30 min prior to the start of reference chemotherapy administration.

| | |
|---|---|
| **Arm title** | Oral NEPA FDC |

Arm description:

Oral netupitant/palonosetron (300 mg/0.50 mg) FDC (Oral NEPA FDC) was to be administered on Day 1 of each cycle. Oral NEPA FDC capsule was to be administered 60 min prior to the start of the reference chemotherapy administration.

| | |
|---|---|
| Arm type | Active comparator |

| | |
|---|---|
| Investigational medicinal product name | Oral netupitant/palonosetron fixed-dose combination (Oral NEPA FDC) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

300 mg netupitant/0.50 mg palonosetron. To be administered 60 min prior to the start of reference chemotherapy administration

| **Number of subjects in period 1** | IV NEPA FDC | Oral NEPA FDC |
|---|---|---|
| Started | 203 | 202 |
| Completed | 120 | 117 |
| Not completed | 83 | 85 |
| Consent withdrawn by subject | 8 | 7 |
| Physician decision | 8 | 12 |
| Adverse event, non-fatal | 16 | 18 |
| Death | 10 | 15 |
| I/E criteria not met for a repeated cycle | 10 | 5 |
| Overall study closure | 24 | 19 |
| Other reasons | 5 | 6 |
| Lost to follow-up | 2 | 3 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | IV NEPA FDC |
| Reporting group description: | |
| IV fosnetupitant/palonosetron (260 mg/0.25 mg) FDC (IV NEPA FDC) was to be administered as a 30-min infusion of a 50-mL solution on Day 1 of each cycle. The 30-min (±5 min) IV NEPA FDC infusion was to be started 30 min prior to the start of the reference chemotherapy administration. The 30-min IV infusion was to be completed before starting chemotherapy administration. | |
| Reporting group title | Oral NEPA FDC |
| Reporting group description: | |
| Oral netupitant/palonosetron (300 mg/0.50 mg) FDC (Oral NEPA FDC) was to be administered on Day 1 of each cycle. Oral NEPA FDC capsule was to be administered 60 min prior to the start of the reference chemotherapy administration. | |

| Reporting group values | IV NEPA FDC | Oral NEPA FDC | Total |
|---|---|---|---|
| Number of subjects | 203 | 202 | 405 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 129 | 133 | 262 |
| From 65-84 years | 74 | 69 | 143 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 60 | 58.9 | |
| standard deviation | ± 9.7 | ± 10.6 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 96 | 94 | 190 |
| Male | 107 | 108 | 215 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | IV NEPA FDC |

Reporting group description:

IV fosnetupitant/palonosetron (260 mg/0.25 mg) FDC (IV NEPA FDC) was to be administered as a 30-min infusion of a 50-mL solution on Day 1 of each cycle. The 30-min (±5 min) IV NEPA FDC infusion was to be started 30 min prior to the start of the reference chemotherapy administration. The 30-min IV infusion was to be completed before starting chemotherapy administration.

| | |
|---|---|
| Reporting group title | Oral NEPA FDC |

Reporting group description:

Oral netupitant/palonosetron (300 mg/0.50 mg) FDC (Oral NEPA FDC) was to be administered on Day 1 of each cycle. Oral NEPA FDC capsule was to be administered 60 min prior to the start of the reference chemotherapy administration.

| | |
|---|---|
| Subject analysis set title | Full Analysis Set: IV NEPA FDC |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Included all randomized patients who received the HEC regimen and active study drug (including partial infusion). Following the intent-to-treat principle, patients were assigned to the treatment group to which they were randomized.

| | |
|---|---|
| Subject analysis set title | Safety population: IV NEPA FDC |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Included all patients who received at least one dose of active study drug (including partial infusion). Patients were assigned to treatment groups according to the actual treatment received.

| | |
|---|---|
| Subject analysis set title | Full Analysis Set: Oral NEPA FDC |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Included all randomized patients who received the HEC regimen and active study drug (including partial infusion). Following the intent-to-treat principle, patients were assigned to the treatment group to which they were randomized.

| | |
|---|---|
| Subject analysis set title | Safety Population: Oral NEPA FDC |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Included all patients who received at least one dose of active study drug (including partial infusion). Patients were assigned to treatment groups according to the actual treatment received.

### Primary: Complete Response in acute phase: Cycle 1

| | |
|---|---|
| End point title | Complete Response in acute phase: Cycle 1 |

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 92.6 (88.2 to 95.5) | 90.5 (85.7 to 93.9) | | |

## Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: Oral NEPA FDC v Full Analysis Set: IV NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 7.2 |

Notes:

[1] - No formal test was planned for this endpoint.

## Primary: Complete Response in delayed phase: Cycle 1

| End point title | Complete Response in delayed phase: Cycle 1 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Primary |
|---|---|

End point timeframe:

Delayed phase (>24-120 h)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 78.3 (72.2 to 83.4) | 87.6 (82.3 to 91.4) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[2] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.8 |
| upper limit | -2.2 |

Notes:

[2] - No formal test was planned for this endpoint.

### Primary: Complete Response in overall phase: Cycle 1

| End point title | Complete Response in overall phase: Cycle 1 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Primary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 76.8 (70.6 to 82.1) | 84.1 (78.4 to 88.5) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[3] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.2 |
| upper limit | -0.1 |

Notes:

[3] - No formal test was planned for this endpoint.

### Secondary: Complete Response in acute phase: Cycle 2

| End point title | Complete Response in acute phase: Cycle 2 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[4] | 176[5] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 89.9 (84.7 to 93.5) | 90.3 (85.1 to 93.9) | | |

Notes:

[4] - Discontinuation after cycle 1

[5] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |

| | |
|---|---|
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[6] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.4 |
| upper limit | 6.3 |

Notes:

[6] - No formal test was planned for this endpoint.

## Secondary: Complete Response in delayed phase: Cycle 2

| | |
|---|---|
| End point title | Complete Response in delayed phase: Cycle 2 |

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[7] | 176[8] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 82.1 (75.9 to 87) | 89.2 (83.8 to 93) | | |

Notes:

[7] - Discontinuation after cycle 1

[8] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[9] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6.4 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.1 |
| upper limit | 0.4 |

Notes:

[9] - No formal test was planned for this endpoint.

## Secondary: Complete Response in overall phase: Cycle 2

| | |
|---|---|
| End point title | Complete Response in overall phase: Cycle 2 |

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Overall phase (0-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[10] | 176[11] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 79.9 (73.4 to 85.1) | 85.8 (79.9 to 90.2) | | |

Notes:

[10] - Discontinuation after cycle 1

[11] - Discontinuation after cycle 1

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[12] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -5.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.7 |
| upper limit | 2 |

Notes:

[12] - No formal test was planned for this endpoint.

## Secondary: Complete Response in acute phase: Cycle 3

| End point title | Complete Response in acute phase: Cycle 3 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[13] | 150[14] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 92.6 (87.6 to 95.7) | 96 (91.5 to 98.2) | | |

Notes:

[13] - Discontinuation after previous cycle

[14] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[15] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 2.4 |

Notes:

[15] - No formal test was planned for this endpoint.

## Secondary: Complete Response in delayed phase: Cycle 3

| End point title | Complete Response in delayed phase: Cycle 3 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[16] | 150[17] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 85.9 (79.7 to 90.4) | 90 (84.2 to 93.8) | | |

Notes:

[16] - Discontinuation after previous cycle

[17] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[18] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 4 |

Notes:

[18] - No formal test was planned for this endpoint.

## Secondary: Complete Response in overall phase: Cycle 3

| End point title | Complete Response in overall phase: Cycle 3 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[19] | 150[20] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 84 (77.7 to 88.9) | 88.7 (82.6 to 92.8) | | |

Notes:

[19] - Discontinuation after previous cycle

[20] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[21] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.1 |
| upper limit | 4.2 |

Notes:

[21] - No formal test was planned for this endpoint.

### Secondary: Complete Response in acute phase: Cycle 4

| End point title | Complete Response in acute phase: Cycle 4 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[22] | 117[23] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.2 (83.6 to 94.3) | 99.1 (95.3 to 99.8) | | |

Notes:

[22] - Discontinuation after previous cycle

[23] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[24] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.9 |
| upper limit | -2.2 |

Notes:

[24] - No formal test was planned for this endpoint.

## Secondary: Complete Response in delayed phase: Cycle 4

| End point title | Complete Response in delayed phase: Cycle 4 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[25] | 117[26] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 86.1 (78.8 to 91.1) | 98.3 (94 to 99.5) | | |

Notes:

[25] - Discontinuation after previous cycle

[26] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[27] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -9.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.4 |
| upper limit | -3.8 |

Notes:

[27] - No formal test was planned for this endpoint.

### Secondary: Complete Response in overall phase: Cycle 4

| End point title | Complete Response in overall phase: Cycle 4 |
|---|---|

End point description:

Complete response in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[28] | 117[29] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 83.6 (76 to 89.1) | 97.4 (92.7 to 99.1) | | |

Notes:

[28] - Discontinuation after previous cycle

[29] - Discontinuation after previous cycle

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[30] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -11.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.6 |
| upper limit | -4.6 |

Notes:

[30] - No formal test was planned for this endpoint.

**Secondary: Absence of Emetic Episodes in acute phase: Cycle 1**

| End point title | Absence of Emetic Episodes in acute phase: Cycle 1 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC].
Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 95.1 (91.2 to 97.3) | 93 (88.6 to 95.8) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |

| | |
|---|---|
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[31] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 2.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.8 |
| upper limit | 6.5 |

Notes:

[31] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in delayed phase: Cycle 1

| | |
|---|---|
| End point title | Absence of Emetic Episodes in delayed phase: Cycle 1 |

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 85.2 (79.7 to 89.4) | 91.5 (86.9 to 94.7) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[32] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6.2 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | -0.4 |

Notes:

[32] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in overall phase: Cycle 1

| | |
|---|---|
| End point title | Absence of Emetic Episodes in overall phase: Cycle 1 |

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Overall phase (0-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 84.2 (78.6 to 88.6) | 88.6 (83.4 to 92.3) | | |

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[33] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -4.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.4 |
| upper limit | 1.8 |

Notes:

[33] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in acute phase: Cycle 2

| End point title | Absence of Emetic Episodes in acute phase: Cycle 2 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[34] | 176[35] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 91.6 (86.6 to 94.9) | 93.8 (89.2 to 96.5) | | |

Notes:

[34] - Discontinuation after cycle 1

[35] - Discontinuation after cycle 1

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[36] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -1.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7 |
| upper limit | 3.2 |

Notes:

[36] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in delayed phase: Cycle 2

| End point title | Absence of Emetic Episodes in delayed phase: Cycle 2 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[37] | 176[38] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 87.2 (81.5 to 91.3) | 94.9 (90.6 to 97.3) | | |

Notes:

[37] - Discontinuation after cycle 1

[38] - Discontinuation after cycle 1

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[39] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.2 |
| upper limit | -2 |

Notes:

[39] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in overall phase: Cycle 2

| End point title | Absence of Emetic Episodes in overall phase: Cycle 2 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[40] | 176[41] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 85.5 (79.6 to 89.9) | 93.2 (88.5 to 96.1) | | |

Notes:

[40] - Discontinuation after cycle 1

[41] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[42] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.8 |
| upper limit | -1.7 |

Notes:

[42] - No formal test was planned for this endpoint.

### Secondary: Absence of Emetic Episodes in acute phase: Cycle 3

| End point title | Absence of Emetic Episodes in acute phase: Cycle 3 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC].
Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[43] | 150[44] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 94.5 (89.8 to 97.1) | 96.7 (92.4 to 98.6) | | |

Notes:

[43] - Discontinuation after previous cycle

[44] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[45] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.7 |
| upper limit | 3 |

Notes:

[45] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in delayed phase: Cycle 3

| End point title | Absence of Emetic Episodes in delayed phase: Cycle 3 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[46] | 150[47] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 92 (86.8 to 95.3) | 93.3 (88.2 to 96.3) | | |

Notes:

[46] - Discontinuation after previous cycle

[47] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[48] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.4 |
| upper limit | 4.8 |

Notes:

[48] - No formal test was planned for this endpoint.

### Secondary: Absence of Emetic Episodes in overall phase: Cycle 3

| End point title | Absence of Emetic Episodes in overall phase: Cycle 3 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[49] | 150[50] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.2 (84.7 to 93.9) | 92.7 (87.3 to 95.9) | | |

Notes:

[49] - Discontinuation after previous cycle

[50] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[51] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.7 |
| upper limit | 4.4 |

Notes:

[51] - No formal test was planned for this endpoint.

### Secondary: Absence of Emetic Episodes in acute phase: Cycle 4

| End point title | Absence of Emetic Episodes in acute phase: Cycle 4 |
|---|---|

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[52] | 117[53] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 92.6 (86.6 to 96.1) | 100 (96.8 to 100) | | |

Notes:

[52] - Discontinuation after previous cycle

[53] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |

| | |
|---|---|
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[54] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.6 |
| upper limit | -2.3 |

Notes:

[54] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in delayed phase: Cycle 4

| | |
|---|---|
| End point title | Absence of Emetic Episodes in delayed phase: Cycle 4 |

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[55] | 117[56] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.2 (83.6 to 94.3) | 99.1 (95.3 to 99.8) | | |

Notes:

[55] - Discontinuation after previous cycle

[56] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[57] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7.5 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.7 |
| upper limit | -2.4 |

Notes:

[57] - No formal test was planned for this endpoint.

## Secondary: Absence of Emetic Episodes in overall phase: Cycle 4

| | |
|---|---|
| End point title | Absence of Emetic Episodes in overall phase: Cycle 4 |

End point description:

Absence of Emetic Episodes in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Overall phase (0-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[58] | 117[59] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 88.5 (81.7 to 93) | 99.1 (95.3 to 99.8) | | |

Notes:

[58] - Discontinuation after previous cycle

[59] - Discontinuation after previous cycle

## Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[60] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -9.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.7 |
| upper limit | -3.7 |

Notes:

[60] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in acute phase: Cycle 1

| End point title | Absence of Rescue Medication in acute phase: Cycle 1 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 96.1 (92.4 to 98) | 93 (88.6 to 95.8) | | |

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[61] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 7.3 |

Notes:

[61] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in delayed phase: Cycle 1

| End point title | Absence of Rescue Medication in delayed phase: Cycle 1 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 84.7 (79.1 to 89) | 91.5 (86.9 to 94.7) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[62] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.9 |
| upper limit | -1 |

Notes:

[62] - No formal test was planned for this endpoint.

**Secondary: Absence of Rescue Medication in overall phase: Cycle 1**

| End point title | Absence of Rescue Medication in overall phase: Cycle 1 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 82.8 (77 to 87.3) | 89.1 (84 to 92.7) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|
| Statistical analysis description: | |
| The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval. | |
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[63] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.3 |
| upper limit | 0.2 |

Notes:

[63] - No formal test was planned for this endpoint.

### Secondary: Absence of Rescue Medication in acute phase: Cycle 2

| End point title | Absence of Rescue Medication in acute phase: Cycle 2 |
|---|---|
| End point description: | |
| Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method. | |
| End point type | Secondary |
| End point timeframe: | |
| Acute phase (0-24 hour) | |

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[64] | 176[65] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 94.4 (90 to 96.9) | 91.5 (86.4 to 94.8) | | |

Notes:

[64] - Discontinuation after cycle 1

[65] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[66] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 3.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 8.9 |

Notes:

[66] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in delayed phase: Cycle 2

| End point title | Absence of Rescue Medication in delayed phase: Cycle 2 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[67] | 176[68] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 87.2 (81.5 to 91.3) | 89.8 (84.4 to 93.4) | | |

Notes:

[67] - Discontinuation after cycle 1

[68] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[69] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.4 |
| upper limit | 4 |

Notes:

[69] - No formal test was planned for this endpoint.

### Secondary: Absence of Rescue Medication in overall phase: Cycle 2

| End point title | Absence of Rescue Medication in overall phase: Cycle 2 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[70] | 176[71] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 85.5 (79.6 to 89.9) | 86.9 (81.2 to 91.1) | | |

Notes:

[70] - Discontinuation after cycle

[71] - Discontinuation after cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[72] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.4 |
| upper limit | 6.1 |

Notes:

[72] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in acute phase: Cycle 3

| End point title | Absence of Rescue Medication in acute phase: Cycle 3 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[73] | 150[74] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 95.7 (91.4 to 97.9) | 96.7 (92.4 to 98.6) | | |

Notes:

[73] - Discontinuation after previous cycle

[74] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |

| | |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[75] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.7 |
| upper limit | 3.5 |

Notes:

[75] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in delayed phase: Cycle 3

| | |
|---|---|
| End point title | Absence of Rescue Medication in delayed phase: Cycle 3 |

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[76] | 150[77] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.8 (85.4 to 94.3) | 90.7 (84.9 to 94.4) | | |

Notes:

[76] - Discontinuation after previous cycle

[77] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[78] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.3 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.4 |
| upper limit | 6.9 |

Notes:

[78] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in overall phase: Cycle 3

| | |
|---|---|
| End point title | Absence of Rescue Medication in overall phase: Cycle 3 |

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Overall phase (0-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[79] | 150[80] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 89.6 (83.9 to 93.4) | 90 (84.2 to 93.8) | | |

Notes:

[79] - Discontinuation after previous cycle

[80] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[81] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.8 |
| upper limit | 6.9 |

Notes:

[81] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in acute phase: Cycle 4

| End point title | Absence of Rescue Medication in acute phase: Cycle 4 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[82] | 117[83] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 93.4 (87.6 to 96.6) | 99.1 (95.3 to 99.8) | | |

Notes:

[82] - Discontinuation after previous cycle

[83] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[84] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -4.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.6 |
| upper limit | -0.4 |

Notes:

[84] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in delayed phase: Cycle 4

| End point title | Absence of Rescue Medication in delayed phase: Cycle 4 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[85] | 117[86] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.2 (83.6 to 94.3) | 98.3 (94 to 99.5) | | |

Notes:

[85] - Discontinuation after previous cycle

[86] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[87] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.8 |
| upper limit | -1.1 |

Notes:

[87] - No formal test was planned for this endpoint.

## Secondary: Absence of Rescue Medication in overall phase: Cycle 4

| End point title | Absence of Rescue Medication in overall phase: Cycle 4 |
|---|---|

End point description:

Absence of Rescue Medication in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[88] | 117[89] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 88.5 (81.7 to 93) | 97.4 (92.7 to 99.1) | | |

Notes:

[88] - Discontinuation after previous cycle

[89] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[90] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -6.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.3 |
| upper limit | -1.1 |

Notes:

[90] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in acute phase: Cycle 1

| End point title | Absence of Significant Nausea in acute phase: Cycle 1 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.1 (85.3 to 93.5) | 93 (88.6 to 95.8) | | |

**Statistical analyses**

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[91] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.6 |
| upper limit | 2.3 |

Notes:

[91] - No formal test was planned for this endpoint.

**Secondary: Absence of Significant Nausea in delayed phase: Cycle 1**

| End point title | Absence of Significant Nausea in delayed phase: Cycle 1 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 81.3 (75.4 to 86) | 89.1 (84 to 92.7) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[92] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.7 |
| upper limit | -0.8 |

Notes:

[92] - No formal test was planned for this endpoint.

### Secondary: Absence of Significant Nausea in overall phase: Cycle 1

| End point title | Absence of Significant Nausea in overall phase: Cycle 1 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 203 | 201 | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 79.3 (73.2 to 84.3) | 86.6 (81.2 to 90.6) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 404 |
| Analysis specification | Pre-specified |
| Analysis type | other[93] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.8 |
| upper limit | -0.2 |

Notes:

[93] - No formal test was planned for this endpoint.

### Secondary: Absence of Significant Nausea in acute phase: Cycle 2

| End point title | Absence of Significant Nausea in acute phase: Cycle 2 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[94] | 176[95] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 91.1 (86 to 94.4) | 93.8 (89.2 to 96.5) | | |

Notes:

[94] - Discontinuation after cycle 1

[95] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |

| | |
|---|---|
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[96] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -1.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7 |
| upper limit | 3.4 |

Notes:

[96] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in delayed phase: Cycle 2

| | |
|---|---|
| End point title | Absence of Significant Nausea in delayed phase: Cycle 2 |

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[97] | 176[98] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 81 (74.6 to 86.1) | 89.2 (83.8 to 93) | | |

Notes:

[97] - Discontinuation after cycle 1

[98] - Discontinuation after cycle 1

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[99] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -8.4 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.1 |
| upper limit | -1.7 |

Notes:

[99] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in overall phase: Cycle 2

| | |
|---|---|
| End point title | Absence of Significant Nausea in overall phase: Cycle 2 |

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Overall phase (0-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 179[100] | 176[101] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 79.9 (73.4 to 85.1) | 86.9 (81.2 to 91.1) | | |

Notes:

[100] - Discontinuation after cycle 1

[101] - Discontinuation after cycle 1

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 355 |
| Analysis specification | Pre-specified |
| Analysis type | other[102] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.4 |
| upper limit | -0.3 |

Notes:

[102] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in acute phase: Cycle 3

| End point title | Absence of Significant Nausea in acute phase: Cycle 3 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[103] | 150[104] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 92.6 (87.6 to 95.7) | 95.3 (90.7 to 97.7) | | |

Notes:

[103] - Discontinuation after previous cycle

[104] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[105] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.3 |
| upper limit | 3.2 |

Notes:

[105] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in delayed phase: Cycle 3

| End point title | Absence of Significant Nausea in delayed phase: Cycle 3 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| **End point values** | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[106] | 150[107] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 86.5 (80.4 to 90.9) | 90 (84.2 to 93.8) | | |

Notes:

[106] - Discontinuation after previous cycle

[107] - Discontinuation after previous cycle

### Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[108] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 4.2 |

Notes:

[108] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in overall phase: Cycle 3

| End point title | Absence of Significant Nausea in overall phase: Cycle 3 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 163[109] | 150[110] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 84 (77.7 to 88.9) | 90 (84.2 to 93.8) | | |

Notes:

[109] - Discontinuation after previous cycle

[110] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[111] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -4.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.8 |
| upper limit | 2.3 |

Notes:

[111] - No formal test was planned for this endpoint.

## Secondary: Absence of Significant Nausea in acute phase: Cycle 4

| End point title | Absence of Significant Nausea in acute phase: Cycle 4 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-24 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Acute phase (0-24 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[112] | 117[113] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 90.2 (83.6 to 94.3) | 94.9 (89.3 to 97.6) | | |

Notes:

[112] - Discontinuation after previous cycle

[113] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[114] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.2 |
| upper limit | 3.3 |

Notes:

[114] - No formal test was planned for this endpoint.

### Secondary: Absence of Significant Nausea in delayed phase: Cycle 4

| End point title | Absence of Significant Nausea in delayed phase: Cycle 4 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting >24-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Delayed phase (>24-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[115] | 117[116] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 87.7 (80.7 to 92.4) | 94.9 (89.3 to 97.6) | | |

Notes:

[115] - Discontinuation after previous cycle

[116] - Discontinuation after previous cycle

### Statistical analyses

| Statistical analysis title | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
|---|---|
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[117] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -5.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.5 |
| upper limit | 1.1 |

Notes:

[117] - No formal test was planned for this endpoint.

### Secondary: Absence of Significant Nausea in overall phase: Cycle 4

| End point title | Absence of Significant Nausea in overall phase: Cycle 4 |
|---|---|

End point description:

Absence of Significant Nausea in the acute phase which is defined as the absence of chemotherapy induced nausea or vomiting 0-120 hour after start of reference highly emetogenic chemotherapy [HEC]. Confidence interval of proportions are obtained by using the Newcombe-Wilson method.

| End point type | Secondary |
|---|---|

End point timeframe:

Overall phase (0-120 hour)

| End point values | Full Analysis Set: IV NEPA FDC | Full Analysis Set: Oral NEPA FDC | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 122[118] | 117[119] | | |
| Units: Proportion | | | | |
| number (confidence interval 95%) | 84.4 (77 to 89.8) | 94 (88.2 to 97.1) | | |

Notes:

[118] - Discontinuation after previous cycle

[119] - Discontinuation after previous cycle

## Statistical analyses

| **Statistical analysis title** | Statistical analysis (FAS) |
|---|---|

Statistical analysis description:

The Cochran-Mantel-Haenszel test stratified by gender and country was used to compare both treatment with a 2-sided 95% confidence interval.

| | |
|---|---|
| Comparison groups | Full Analysis Set: IV NEPA FDC v Full Analysis Set: Oral NEPA FDC |
| Number of subjects included in analysis | 239 |
| Analysis specification | Pre-specified |
| Analysis type | other[120] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | 0.1 |

Notes:

[120] - No formal test was planned for this endpoint.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Informed consent signature or day 1 of each cycle up to the follow-up visit contact which is a maximum of 35 days for each cycle. The study contains four (4) cycles with a 21 day interval between consecutive cycles.

Adverse event reporting additional description:

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship wit h this treatment.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Oral NEPA FDC |

Reporting group description:

Oral netupitant/palonosetron (300 mg/0.50 mg) FDC (Oral NEPA FDC) was to be administered on Day 1 of each cycle. Oral NEPA FDC capsule was to be administered 60 min prior to the start of the reference chemotherapy administration.

| | |
|---|---|
| Reporting group title | IV NEPA FDC |

Reporting group description:

IV fosnetupitant/palonosetron (260 mg/0.25 mg) FDC (IV NEPA FDC) was to be administered as a 30-min infusion of a 50-mL solution on Day 1 of each cycle. The 30-min (±5 min) IV NEPA FDC infusion was to be started 30 min prior to the start of the reference chemotherapy administration. The 30-min IV infusion was to be completed before starting chemotherapy administration.

| **Serious adverse events** | Oral NEPA FDC | IV NEPA FDC | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 201 (0.00%) | 0 / 203 (0.00%) | |
| number of deaths (all causes) | 14 | 10 | |
| number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | Oral NEPA FDC | IV NEPA FDC | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 170 / 201 (84.58%) | 161 / 203 (79.31%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 24 / 201 (11.94%) | 15 / 203 (7.39%) | |
| occurrences (all) | 43 | 25 | |

| | | | |
|---|---|---|---|
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 19 / 201 (9.45%) | 12 / 203 (5.91%) | |
| occurrences (all) | 30 | 17 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 6 / 201 (2.99%) | 11 / 203 (5.42%) | |
| occurrences (all) | 10 | 15 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 13 / 201 (6.47%) | 8 / 203 (3.94%) | |
| occurrences (all) | 16 | 12 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 9 / 201 (4.48%) | 11 / 203 (5.42%) | |
| occurrences (all) | 21 | 19 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 34 / 201 (16.92%) | 33 / 203 (16.26%) | |
| occurrences (all) | 52 | 54 | |
| Leukopenia | | | |
| subjects affected / exposed | 21 / 201 (10.45%) | 21 / 203 (10.34%) | |
| occurrences (all) | 35 | 28 | |
| Neutropenia | | | |
| subjects affected / exposed | 52 / 201 (25.87%) | 57 / 203 (28.08%) | |
| occurrences (all) | 81 | 89 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 17 / 201 (8.46%) | 13 / 203 (6.40%) | |
| occurrences (all) | 26 | 16 | |
| Fatigue | | | |
| subjects affected / exposed | 17 / 201 (8.46%) | 17 / 203 (8.37%) | |
| occurrences (all) | 32 | 30 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 26 / 201 (12.94%) | 21 / 203 (10.34%) | |
| occurrences (all) | 30 | 29 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 14 / 201 (6.97%)<br>20 | 20 / 203 (9.85%)<br>28 | |
| Skin and subcutaneous tissue disorders<br>Alopecia<br>subjects affected / exposed<br>occurrences (all) | <br><br>29 / 201 (14.43%)<br>31 | <br><br>32 / 203 (15.76%)<br>35 | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | <br><br>11 / 201 (5.47%)<br>14 | <br><br>7 / 203 (3.45%)<br>7 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 27 July 2015 | The following change to the study protocol is implemented to comply with a request from the US Food and Drug Administration: - During the conduct of the study, a Data Safety Monitoring Board (DSMB) will periodically review safety data. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported