



Clinical trial results:

A Phase III, Randomized, Placebo-Controlled Clinical Trial to Study the Efficacy and Safety of MK-0517/Fosaprepitant and Ondansetron Versus Ondansetron for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in Pediatric Subjects Receiving Emetogenic Chemotherapy

Summary

EudraCT number	2014-001783-34
Trial protocol	SE NO ES LT FI PT EE HU GB NL GR Outside EU/EEA
Global end of trial date	24 February 2017

Results information

Result version number	v1 (current)
This version publication date	03 September 2017
First version publication date	03 September 2017

Trial information

Trial identification

Sponsor protocol code	0517-044
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02519842
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Registration Number: MK-0517-044, IND Number: 48,924

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 February 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of fosaprepitant (MK-0517) plus ondansetron versus ondansetron alone for the prevention of chemotherapy-induced nausea and vomiting (CINV) in pediatric participants scheduled to receive chemotherapeutic agent(s) associated with moderate or high risk of causing emesis (vomiting), or chemotherapy agent(s) not previously tolerated due to vomiting. The primary hypothesis was that a single dose of fosaprepitant in combination with ondansetron provided superior control of CINV compared to ondansetron alone as measured by the percentage of participants with a Complete Response (no vomiting, no retching, and no use of rescue medications) in the delayed phase (>24 to 120 hours) following initiation of emetogenic chemotherapy in Cycle 1.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. Participants <12 years of age were not permitted to participate in the current study until Pharmacokinetic/Pharmacodynamic and safety data were evaluated from an earlier study to confirm the planned dose adjustments for subjects <12 years of age.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Colombia: 6
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Greece: 10
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Lithuania: 8
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Russian Federation: 2

Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	75
EEA total number of subjects	45

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)	37
Adolescents (12-17 years)	38
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible participants for chemotherapy Cycles 1-6 were 0-17 years old and had documented malignancies and were scheduled to receive chemotherapeutic agent(s) associated with moderate or high risk of emetogenicity. Participants entering Cycles 2-6 must have completed Cycle 1 and had no unresolved drug related adverse events.

Pre-assignment

Screening details:

Participants received double-blinded fosaprepitant+ondansetron with/without dexamethasone OR placebo+ondansetron with/without dexamethasone in Cycle 1. Upon completion of Cycle 1, participants from both Cycle 1 arms had the option to continue for up to 5 cycles of open-label fosaprepitant+5-hydroxytryptamine 3 antagonist with/without dexamethasone.

Period 1

Period 1 title	Base Study-Cycle 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Fosaprepitant Regimen Cycle 1

Arm description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) administered intravenously (IV) on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose of fosaprepitant 150 mg (or age-based adjustment) administered IV on Day 1 prior to chemotherapy

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone administered IV, as specified by local labeling and/or local standard of care, at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy

Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ondansetron administered IV, as specified by local labeling and/or local standard of care, on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy

Arm title	Control Regimen Cycle 1
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Arm description:

Participants received a single dose of matched placebo for fosaprepitant IV on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Arm type	Placebo
Investigational medicinal product name	Placebo for fosaprepitant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single dose of Placebo for fosaprepitant administered IV on Day 1 prior to chemotherapy

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone administered IV, as specified by local labeling and/or local standard of care, at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy

Investigational medicinal product name	Ondansetron
Investigational medicinal product code	
Other name	Ondansetron hydrochloride Zofran® Injection
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ondansetron administered IV, as specified by local labeling and/or local standard of care, on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy

Number of subjects in period 1	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1
Started	38	37
Treated	37	34
Completed	36	34
Not completed	2	3
Non-Compliance with Study Drug	-	1
Adverse event, non-fatal	1	-
Screening Failure	1	1
Withdrawn By Parent/Guardian	-	1

Period 2

Period 2 title	Optional Extension-Cycles 2-6
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Fosaprepitant Regimen Cycles 2-6
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Arm description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) IV on Day 1 prior to chemotherapy plus a 5-hydroxytryptamine 3 (5-HT3) antagonist on Day 1 prior to chemotherapy and per product label or standard of care. Participants may also have received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant
Investigational medicinal product code	
Other name	Emend® for injection fosaprepitant dimeglumine MK-0517
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose of fosaprepitant 150 mg (or age-based adjustment) administered IV on Day 1 prior to chemotherapy

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dexamethasone administered by a route of administration determined by the investigator, as specified by local labeling and/or local standard of care, at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy

Investigational medicinal product name	5-hydroxytryptamine 3 antagonist
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5-HT3 antagonist administered by a route of administration determined by the investigator, as specified by local labeling and/or local standard of care, on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy

Number of subjects in period 2^[1]	Fosaprepitant Regimen Cycles 2-6
Started	55
Completed	26
Not completed	29
Consent withdrawn by subject	1
Physician decision	5
Did not respond to chemotherapy	2
Completed chemotherapy	13
Enrollment Terminated at Site	1
Adverse event, non-fatal	1
Death	1
Withdrawn By Parent/Guardian	3
Cycle Inclusion/Exclusion Criteria Not Met	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Upon completion of Cycle 1, participants from the fosaprepitant and control arms of Cycle 1 had the option to continue in the fosaprepitant arm in Cycles 2-6.

Baseline characteristics

Reporting groups

Reporting group title	Fosaprepitant Regimen Cycle 1
Reporting group description:	
Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) administered intravenously (IV) on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.	
Reporting group title	Control Regimen Cycle 1
Reporting group description:	
Participants received a single dose of matched placebo for fosaprepitant IV on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.	

Reporting group values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1	Total
Number of subjects	38	37	75
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	19	18	37
Adolescents (12-17 years)	19	19	38
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	10.8	10.9	
standard deviation	± 4.2	± 4.4	-
Gender Categorical Units: Subjects			
Female	14	16	30
Male	24	21	45

End points

End points reporting groups

Reporting group title	Fosaprepitant Regimen Cycle 1
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Reporting group description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) administered intravenously (IV) on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Reporting group title	Control Regimen Cycle 1
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Reporting group description:

Participants received a single dose of matched placebo for fosaprepitant IV on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Reporting group title	Fosaprepitant Regimen Cycles 2-6
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Reporting group description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) IV on Day 1 prior to chemotherapy plus a 5-hydroxytryptamine 3 (5-HT₃) antagonist on Day 1 prior to chemotherapy and per product label or standard of care. Participants may also have received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Subject analysis set title	Fosaprepitant Regimen Cycle 1
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) administered intravenously (IV) on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Analysis was in the intent-to-treat population which consists of all randomized participants who received any study drug.

Subject analysis set title	Control Regimen Cycle 1
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

Participants received a single dose of matched placebo for fosaprepitant IV on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Analysis was in the intent-to-treat population which consists of all randomized participants who received any study placebo.

Subject analysis set title	Fosaprepitant Regimen Cycle 1
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) administered intravenously (IV) on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Analysis was in the all subjects as treated population which consists of all randomized participants who received at least one dose of study drug.

Subject analysis set title	Control Regimen Cycle 1
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Participants received a single dose of matched placebo for fosaprepitant IV on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Analysis was in the all subjects as treated population which consists of all randomized participants who received at least one dose of study drug.

Subject analysis set title	Fosaprepitant Regimen Cycles 2-6
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) IV on Day 1 prior to chemotherapy plus a 5-hydroxytryptamine 3 (5-HT₃) antagonist on Day 1 prior to chemotherapy and per product label or standard of care. Participants may also have received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Analysis was in the all subjects as treated population which consists of all randomized participants who received at least one dose of study drug.

Primary: Percentage of Participants Who Experience a Complete Response During the Delayed Phase (>24 to 120 hours post initiation of chemotherapy) in Cycle 1

End point title	Percentage of Participants Who Experience a Complete Response During the Delayed Phase (>24 to 120 hours post initiation of chemotherapy) in Cycle 1 ^[1]
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End point description:

Complete Response was defined as no vomiting, no retching, and no use of rescue medication following the initiation of emetogenic chemotherapy in Cycle 1. A vomiting episode was specified as one or more episodes of emesis (expulsion of stomach contents through the mouth) or retching/dry heaves (an attempt to vomit that is not productive of stomach contents). Distinct vomiting episodes were separated by the absence of emesis and retching for at least one minute. The date and time of each vomiting episode was recorded by participants in diaries at the time of occurrence. The percentage of participants with no vomiting and no retching episodes in the delayed phase, defined as the time period of >24 to 120 hours post initiation of chemotherapy in Cycle 1, was calculated. The endpoint was based on all participants who received at least 1 dose of study drug during Cycle 1.

End point type	Primary
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End point timeframe:

>24 to 120 hours post initiation of chemotherapy (1 to 15 days after the dose of study drug)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Early termination of the study limited the data for efficacy and statistical analyses were not performed for this endpoint.

End point values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	37	34		
Units: percentage of participants				
number (not applicable)	48.6	41.2		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Experience One or More Adverse Events

End point title	Percentage of Participants Who Experience One or More Adverse Events
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End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. The endpoint was based on all participants who received at least 1 dose of study drug during Cycles 1 through 6. An analysis was performed on Tier 2 AEs in Cycle 1 to compare the percentage of participants who received fosaprepitant regimen and experienced at least 1 Tier 2 AE compared with the percentage of participants in the control regimen. The Tier 2 endpoint included broad clinical and laboratory AE categories consisting of the percentage of participants

with any AE, drug-related AE, serious AE, and AEs that are both drug-related and serious. Tier 2 AEs were not pre-specified as events of interest and inclusion in the Tier 2 analysis required that at least 4 participants in any treatment group exhibited the AE.

End point type	Primary
End point timeframe:	
Up to 6.5 months (Up to 2 weeks after last dose of study drug)	

End point values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1	Fosaprepitant Regimen Cycles 2-6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	34	55	
Units: percentage of participants				
number (not applicable)	89.2	79.4	78.2	

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
Statistical analysis description:	
Mean difference in percentage of participants who experienced at least 1 tier 2 AE and received fosaprepitant regimen compared with participants who received control regimen. Estimates were based on the Miettinen & Nurminen method.	
Comparison groups	Fosaprepitant Regimen Cycle 1 v Control Regimen Cycle 1
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	27.9

Primary: Percentage of Participants Who Discontinue Study Drug Due to an Adverse Event

End point title	Percentage of Participants Who Discontinue Study Drug Due to an Adverse Event
End point description:	
An AE is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study drug, whether or not it is considered related to the study drug. The endpoint was based on all participants who received at least 1 dose of study drug during Cycles 1 through 6. An analysis was performed to compare the percentage of participants who discontinued in Cycle 1 due to an AE and received fosaprepitant regimen compared with the percentage of participants who received control regimen.	
End point type	Primary

End point timeframe:

Up to 6 months (Up to last dose of study drug)

End point values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1	Fosaprepitant Regimen Cycles 2-6	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	37	34	55	
Units: percentage of participants				
number (not applicable)	5.4	0	0	

Statistical analyses

Statistical analysis title	Difference in Percentage of Participants
Statistical analysis description: Mean difference in percentage of participants who discontinued due to an AE and received fosaprepitant regimen compared with participants who received control regimen. Estimates were based on the Miettinen & Nurminen method.	
Comparison groups	Fosaprepitant Regimen Cycle 1 v Control Regimen Cycle 1
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	17.8

Secondary: Percentage of Participants Who Experience a Complete Response During the Acute Phase (0 to 24 hours post initiation of chemotherapy) in Cycle 1

End point title	Percentage of Participants Who Experience a Complete Response During the Acute Phase (0 to 24 hours post initiation of chemotherapy) in Cycle 1
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End point description:

Complete Response was defined as no vomiting, no retching, and no use of rescue medication following the initiation of emetogenic chemotherapy in Cycle 1. A vomiting episode was specified as one or more episodes of emesis (expulsion of stomach contents through the mouth) or retching/dry heaves (an attempt to vomit that is not productive of stomach contents). Distinct vomiting episodes were separated by the absence of emesis and retching for at least one minute. The date and time of each vomiting episode was recorded by participants in diaries at the time of occurrence. The percentage of participants with no vomiting and no retching episodes in the acute phase, defined as the time period of 0 to 24 hours post initiation of chemotherapy in Cycle 1, was calculated. The endpoint was based on all participants who received at least 1 dose of study drug during Cycle 1.

End point type	Secondary
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End point timeframe:

0 to 24 hours post initiation of chemotherapy (up to 1 day after the dose of study drug)

End point values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	37	34		
Units: percentage of participants				
number (not applicable)	70.3	58.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experience a Complete Response During the Overall Phase (0 to 120 hours post initiation of chemotherapy) in Cycle 1

End point title	Percentage of Participants Who Experience a Complete Response During the Overall Phase (0 to 120 hours post initiation of chemotherapy) in Cycle 1
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End point description:

Complete Response was defined as no vomiting, no retching, and no use of rescue medication following the initiation of emetogenic chemotherapy in Cycle 1. A vomiting episode was specified as one or more episodes of emesis (expulsion of stomach contents through the mouth) or retching/dry heaves (an attempt to vomit that is not productive of stomach contents). Distinct vomiting episodes were separated by the absence of emesis and retching for at least one minute. The date and time of each vomiting episode was recorded by participants in diaries at the time of occurrence. The percentage of participants with no vomiting and no retching episodes in the overall phase, defined as the time period of 0 to 120 hours post initiation of chemotherapy in Cycle 1, was calculated. The endpoint was based on all participants who received at least 1 dose of study drug during Cycle 1.

End point type	Secondary
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End point timeframe:

0 to 120 hours post initiation of chemotherapy (up to 15 days after the dose of study drug)

End point values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	37	34		
Units: percentage of participants				
number (not applicable)	40.5	32.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experience No Vomiting, Regardless of

Rescue Medication Use, During the Overall Phase (0 to 120 hours post initiation of chemotherapy) in Cycle 1

End point title	Percentage of Participants Who Experience No Vomiting, Regardless of Rescue Medication Use, During the Overall Phase (0 to 120 hours post initiation of chemotherapy) in Cycle 1
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End point description:

Vomiting was assessed, regardless of rescue medicine use, following the initiation of emetogenic chemotherapy in Cycle 1. A vomiting episode was specified as one or more episodes of emesis (expulsion of stomach contents through the mouth) or retching/dry heaves (an attempt to vomit that is not productive of stomach contents). Distinct vomiting episodes were separated by the absence of emesis and retching for at least one minute. The date and time of each vomiting episode was recorded by participants in diaries at the time of occurrence. Rescue medication was permitted to alleviate symptoms of established nausea or vomiting; but not as preventive medication. The percentage of participants with no vomiting and no retching episodes in the overall phase, defined as the time period of 0 to 120 hours post initiation of chemotherapy in Cycle 1, was calculated. The endpoint was based on all participants who received at least 1 dose of study drug during Cycle 1.

End point type	Secondary
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End point timeframe:

0 to 120 hours post initiation of chemotherapy (up to 15 days after the dose of study drug)

End point values	Fosaprepitant Regimen Cycle 1	Control Regimen Cycle 1		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	37	34		
Units: percentage of participants				
number (not applicable)	40.5	32.4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events data were collected up to 6.5 months (from start of study drug and up to 14 days after the last dose for each cycle in Cycles 1-6).

Adverse event reporting additional description:

This safety analysis was based on all participants who received at least 1 dose of study drug during Cycles 1 through 6.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Fosaprepitant Regimen Cycle 1
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Reporting group description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) administered intravenously (IV) on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Reporting group title	Fosaprepitant Regimen Cycles 2-6
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Reporting group description:

Participants received a single dose of fosaprepitant 150 mg (or age-based adjustment) IV on Day 1 prior to chemotherapy plus a 5- hydroxytryptamine 3 (5-HT3) antagonist on Day 1 prior to chemotherapy and per product label or standard of care. Participants may also have received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Reporting group title	Control Regimen Cycle 1
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Reporting group description:

Participants received a single dose of matched placebo for fosaprepitant IV on Day 1 prior to chemotherapy plus ondansetron IV on Day 1 prior to chemotherapy and at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy. Participants may have also received dexamethasone IV at investigator's discretion on day(s) of chemotherapy and up to 24 hours after chemotherapy.

Serious adverse events	Fosaprepitant Regimen Cycle 1	Fosaprepitant Regimen Cycles 2-6	Control Regimen Cycle 1
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 37 (29.73%)	28 / 55 (50.91%)	8 / 34 (23.53%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Tachycardia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 55 (3.64%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	1 / 37 (2.70%)	3 / 55 (5.45%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	4 / 37 (10.81%)	19 / 55 (34.55%)	5 / 34 (14.71%)
occurrences causally related to treatment / all	0 / 4	0 / 32	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 37 (2.70%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Thrombocytopenia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 55 (3.64%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Complication associated with device			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 37 (0.00%)	2 / 55 (3.64%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Soft tissue mass			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Klebsiella bacteraemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 55 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 55 (3.64%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Product issues			
Thrombosis in device			
subjects affected / exposed	1 / 37 (2.70%)	0 / 55 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diet refusal			
subjects affected / exposed	0 / 37 (0.00%)	1 / 55 (1.82%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Fosaprepitant Regimen Cycle 1	Fosaprepitant Regimen Cycles 2-6	Control Regimen Cycle 1
Total subjects affected by non-serious adverse events subjects affected / exposed	28 / 37 (75.68%)	30 / 55 (54.55%)	18 / 34 (52.94%)
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	3 / 55 (5.45%) 3	3 / 34 (8.82%) 3
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	2 / 55 (3.64%) 3	2 / 34 (5.88%) 2
Neutrophil count decreased subjects affected / exposed occurrences (all)	6 / 37 (16.22%) 6	2 / 55 (3.64%) 2	3 / 34 (8.82%) 3
Platelet count decreased subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	5 / 55 (9.09%) 32	3 / 34 (8.82%) 5
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	11 / 37 (29.73%) 11	11 / 55 (20.00%) 20	3 / 34 (8.82%) 3
Febrile neutropenia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	2 / 55 (3.64%) 2	2 / 34 (5.88%) 2
Leukopenia subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 5	7 / 55 (12.73%) 15	0 / 34 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	5 / 37 (13.51%) 6	4 / 55 (7.27%) 5	3 / 34 (8.82%) 3
Thrombocytopenia subjects affected / exposed occurrences (all)	8 / 37 (21.62%) 8	7 / 55 (12.73%) 14	2 / 34 (5.88%) 2
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 55 (1.82%) 2	2 / 34 (5.88%) 2

Mucosal inflammation subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 4	4 / 55 (7.27%) 6	0 / 34 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 5	7 / 55 (12.73%) 8	0 / 34 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	6 / 55 (10.91%) 9	1 / 34 (2.94%) 1
Constipation subjects affected / exposed occurrences (all)	3 / 37 (8.11%) 3	5 / 55 (9.09%) 6	2 / 34 (5.88%) 3
Diarrhoea subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 55 (1.82%) 1	0 / 34 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	9 / 55 (16.36%) 14	1 / 34 (2.94%) 1
Proctalgia subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	3 / 55 (5.45%) 3	0 / 34 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1	3 / 55 (5.45%) 3	0 / 34 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	4 / 37 (10.81%) 4	11 / 55 (20.00%) 24	1 / 34 (2.94%) 1
Respiratory, thoracic and mediastinal disorders			
Epistaxis subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 55 (1.82%) 3	0 / 34 (0.00%) 0
Hiccups subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 55 (0.00%) 0	1 / 34 (2.94%) 1
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 55 (0.00%) 0	1 / 34 (2.94%) 1
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	0 / 55 (0.00%) 0	0 / 34 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	2 / 37 (5.41%) 2	1 / 55 (1.82%) 1	1 / 34 (2.94%) 1
Bone pain subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0	1 / 55 (1.82%) 1	2 / 34 (5.88%) 2
Pain in extremity subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 2	4 / 55 (7.27%) 4	1 / 34 (2.94%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Enrollment was terminated early because it was determined that data were not necessary to support a claim in pediatric participants. The last participant was enrolled on 2016-08-05. Enrolled participants were allowed to remain active in the study.

Notes: