Clinical trial results:
A Phase 4, Open-label, Single Arm Study to Evaluate the Safety and Tolerability of a Three-day Fosaprepitant Regimen Administered for the Prevention of Chemotherapy-Induced Nausea and Vomiting (CINV) in Pediatric Participants Receiving Emetogenic Chemotherapy

Summary

EudraCT number	2018-004844-43
Trial protocol	GB LT PL HU NL GR
Global end of trial date	11 February 2021

Results information

Result version number	v1 (current)
This version publication date	19 August 2021
First version publication date	19 August 2021

Trial information

Trial identification

Sponsor protocol code	0517-045

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04054193
WHO universal trial number (UTN)	-

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	11 February 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 February 2021
Global end of trial reached?	Yes
Global end of trial date	11 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and tolerability of a 3-day intravenous (IV) fosaprepitant (MK-0517) regimen for the prevention of CINV in pediatric participants scheduled to receive emetogenic chemotherapy.

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 September 2019
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	Greece: 15
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Lithuania: 11
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Peru: 19
Worldwide total number of subjects	103
EEA total number of subjects	53

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)	15
Children (2-11 years)	57
Adolescents (12-17 years)	31
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible participants were recruited at 25 study sites in 9 countries. All participants were enrolled for Cycle 1 on which the primary objective was based.

Pre-assignment

Screening details:

Upon completion of Cycle 1, participants were given the option to exit the study and be considered completed, or to continue on study therapy for up to 2 more (optional) cycles (3 days of treatment + 14 days of follow-up per cycle) of chemotherapy where fosarepitant was administered and additional safety data collected.

Period 1

Period 1 title	Cycle 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Fosarepitant Cycle 1

Arm description:

Participants received fosarepitant dimeglumine once daily (QD) for 3 days during Cycle 1 and were followed for 14 days. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy.

Arm type	Experimental
Investigational medicinal product name	Fosaprepitant dimeglumine
Investigational medicinal product code	
Other name	MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants 6 months to <12 years of age received fosarepitant dimeglumine 3.0 mg/kg on Day 1 and 2.0 mg/kg on Days 2 and 3. Participants 12 to 17 years of age received fosarepitant dimeglumine 115 mg on Day 1 and 80 mg on Days 2 and 3.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received optional dexamethasone at the investigator's discretion according to product label or standard of care.

Investigational medicinal product name	5-HT3 Antagonist
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All participants received a 5-hydroxytryptamine (serotonin; [5-HT]) 3 receptor antagonist on Day 1 and had the option to take on Days 2-3. The dose was as per product label or standard of care.

Number of subjects in period 1	Fosarepitant Cycle 1
Started	103
Treated (≥1 dose)	100
Completed	98
Not completed	5
Allocated but not treated	3
Physician decision	1
Consent withdrawn by parent/guardian	1

Period 2

Period 2 title	Cycles 2-3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Fosarepitant Cycles 2-3

Arm description:

Participants received fosarepitant dimeglumine once daily (QD) for 3 days and were followed for 14 days during Cycles 2-3. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy, of each cycle.

Arm type	Experimental
Investigational medicinal product name	Fosarepitant
Investigational medicinal product code	
Other name	MK-0517
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants 6 months to <12 years of age received fosarepitant 3.0 mg/kg on Day 1 and 2.0 mg/kg on Days 2 and 3. Participants 12 to 17 years of age received fosarepitant 115 mg on Day 1 and 80 mg on Days 2 and 3.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received optional dexamethasone at the investigator's discretion according to product label or standard of care.

Investigational medicinal product name	5-HT3 Antagonist
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All participants received a 5-hydroxytryptamine (serotonin; [5-HT]) 3 receptor antagonist on Day 1 and

had the option to take on Days 2-3. The dose was as per product label or standard of care.

Number of subjects in period 2[1]	Fosarepitant Cycles 2-3
Started	69
Completed	48
Not completed	21
Physician decision	2
Consent withdrawn by parent/guardian	2
Various reasons	17

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 (upon which the study objectives are based), participants had the option to exit the study and be considered completed, or to continue on for up to 2 additional treatment cycles.

Baseline characteristics

Reporting groups	
Reporting group title	Fosarepitant Cycle 1
Reporting group description:	
Participants received fosarepitant dimeglumine once daily (QD) for 3 days during Cycle 1 and were followed for 14 days. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy.	

Reporting group values	Fosarepitant Cycle 1	Total	
Number of subjects	103	103	
Age Categorical Units: Subjects			
Infants and toddlers (28 days - 23 months)	15	15	
Children (2 to 11 years)	57	57	
Adolescents (12 to 17 years)	31	31	
Age Continuous Units: years			
arithmetic mean	7.7		
standard deviation	± 5.0	-	
Gender Categorical Units: Subjects			
Female	50	50	
Male	53	53	
Race Units: Subjects			
American Indian Or Alaska Native	14	14	
Black Or African American	2	2	
Multiple	6	6	
White	81	81	
Ethnicity Units: Subjects			
Hispanic Or Latino	22	22	
Not Hispanic Or Latino	77	77	
Not Reported	1	1	
Unknown	3	3	

End points

End points reporting groups

Reporting group title	Fosarepitant Cycle 1

Reporting group description:

Participants received fosarepitant dimeglumine once daily (QD) for 3 days during Cycle 1 and were followed for 14 days. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy.

Reporting group title	Fosarepitant Cycles 2-3

Reporting group description:

Participants received fosarepitant dimeglumine once daily (QD) for 3 days and were followed for 14 days during Cycles 2-3. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy, of each cycle.

Primary: Percentage of Participants Who Experienced One or More Adverse Events (AEs) During Cycle 1

End point title	Percentage of Participants Who Experienced One or More Adverse Events (AEs) During Cycle 1[1]

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 percentage of participants who experience one or more AE(s) during Cycle 1 is presented. The analysis population consists of all allocated participants who received ≥1 dose of study intervention.

End point type	Primary

End point timeframe:

Up to 22 days

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: Per protocol, only descriptive statistics are presented.

End point values	Fosarepitant Cycle 1			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of Participants				
number (not applicable)	80.0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event (AE) During Cycle 1

End point title	Percentage of Participants Who Discontinued Study Drug Due to an Adverse Event (AE) During Cycle 1[2]

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 percentage of participants who discontinue study treatment due to an AE during Cycle 1 is presented. The analysis population consists of all allocated participants who received ≥1 dose of study intervention.

End point type	Primary

End point timeframe:

Up to 3 days

Notes:

[2] - 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: Per protocol, only descriptive statistics are presented.

End point values	Fosarepitant Cycle 1			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of Participants				
number (not applicable)	2.0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to approximately 3.5 months	
Adverse event reporting additional description:	
All allocated participants who received ≥1 dose of study intervention are included.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Fosarepitant Cycle 1
Reporting group description:	
Participants received fosarepitant dimeglumine once daily (QD) for 3 days during Cycle 1 and were followed for 14 days. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy.	
Reporting group title	Fosarepitant Cycles 2-3
Reporting group description:	
Participants received fosarepitant dimeglumine once daily (QD) for 3 days and were followed for 14 days during Cycles 2-3. Participants also optionally received dexamethasone as background therapy, and a 5-HT3 receptor antagonist on Day 1 and optionally on Days 2-3 as background therapy, of each cycle.	

Serious adverse events	Fosarepitant Cycle 1	Fosarepitant Cycles 2-3	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 100 (30.00%)	27 / 69 (39.13%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Coordination abnormal			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 100 (1.00%)	4 / 69 (5.80%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	17 / 100 (17.00%)	15 / 69 (21.74%)	
occurrences causally related to treatment / all	0 / 18	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 100 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 100 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 100 (0.00%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematotoxicity			
subjects affected / exposed	1 / 100 (1.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 100 (1.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 100 (1.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 100 (1.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 100 (2.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	2 / 100 (2.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 100 (1.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 100 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungaemia			

subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 100 (1.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fosarepitant Cycle 1	Fosarepitant Cycles 2-3	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 100 (64.00%)	27 / 69 (39.13%)	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	14 / 100 (14.00%)	2 / 69 (2.90%)	
occurrences (all)	14	2	
Platelet count decreased			
subjects affected / exposed	9 / 100 (9.00%)	4 / 69 (5.80%)	
occurrences (all)	9	4	
White blood cell count decreased			
subjects affected / exposed	7 / 100 (7.00%)	1 / 69 (1.45%)	
occurrences (all)	8	1	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	24 / 100 (24.00%)	7 / 69 (10.14%)	
occurrences (all)	28	8	
Haematotoxicity			
subjects affected / exposed	9 / 100 (9.00%)	10 / 69 (14.49%)	
occurrences (all)	9	15	
Neutropenia			
subjects affected / exposed	15 / 100 (15.00%)	4 / 69 (5.80%)	
occurrences (all)	16	4	
Thrombocytopenia			
subjects affected / exposed	11 / 100 (11.00%)	3 / 69 (4.35%)	
occurrences (all)	11	3	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 100 (6.00%)	3 / 69 (4.35%)	
occurrences (all)	6	3	
Nausea			
subjects affected / exposed	24 / 100 (24.00%)	8 / 69 (11.59%)	
occurrences (all)	25	9	
Vomiting			
subjects affected / exposed	16 / 100 (16.00%)	8 / 69 (11.59%)	
occurrences (all)	18	13	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 100 (6.00%)	0 / 69 (0.00%)	
occurrences (all)	6	0	

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

None reported