Clinical trial results:
A Phase 3 Study to Evaluate the Efficacy and Safety of Dinaciclib or Ofatumumab in Subjects With Refractory Chronic Lymphocytic Leukemia

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2011-005186-20
Trial protocol	NO CZ SE FI LT LV ES HU IT PL BE GR EE SK
Global end of trial date	22 December 2014

Results information

Result version number	v1 (current)
This version publication date	01 July 2016
First version publication date	01 July 2016

Trial information

Trial identification

Sponsor protocol code	P07714

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01580228
WHO universal trial number (UTN)	-
Other trial identifiers	Merck: MK-7965-012

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2014
Global end of trial reached?	Yes
Global end of trial date	22 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was conducted to demonstrate the superiority in progression-free survival (PFS) of dinaciclib compared to ofatumumab in chronic lymphocytic leukemia (CLL) participants with deletion 17p (del 17p) gene mutation or in the overall population who are refractory to either fludarabine treatment or chemoimmunotherapy.

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	06 August 2012
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	Australia: 1
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	New Zealand: 9
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	44
EEA total number of subjects	28

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)	25
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with CLL, who were refractory to either fludarabine treatment or chemoimmunotherapy and met the eligibility criteria for the trial, were stratified by del 17 status, refractory/relapse status of the prior therapy, and risk assessment for tumor lysis syndrome (TLS), and randomized to one of 2 arms, dinaciclib or ofatumumab.

Pre-assignment

Screening details:

This study enrolled males and females with a confirmed diagnosis of CLL, as defined by the 2008 International Workshop on Chronic Lymphocytic Leukemia (iwCLL) criteria. In addition, participants must have had fludarabine or chemoimmunotherapy refractory disease.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dinaciclib

Arm description:

Participants received dinaciclib, administered intravenously, over 2 hours at a dose of 7 mg/m^2 on Day 1, 10 mg/m^2 on Day 8, and 14 mg/m^2 on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m^2 on Days 1, 8, and 15 of each 28-day cycle for a total of 12 cycles.

Arm type	Experimental
Investigational medicinal product name	Dinaciclib
Investigational medicinal product code	
Other name	MK-7965, SCH 727965
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dinaciclib administered intravenously over 2 hours at a dose of 7 mg/m^2 on Day 1, 10 mg/m^2 on Day 8, and 14 mg/m^2 on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m^2 on Days 1, 8, and 15 of each 28-day cycle for a total of 12 cycles.

Arm title	Ofatumumab

Arm description:

Participants received ofatumumab, administered intravenously, at a dose of 300 mg on Cycle 1 Day 1, followed by 2000 mg on Cycle 1 Days 8, 15, and 22; Cycle 2 Days 1, 8, 15, and 22; followed 5 weeks later on Day 1 of Cycles 4-12.

Arm type	Active comparator
Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	
Other name	Arzerra®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab administered intravenously at a dose of 300 mg on Cycle 1 Day 1, followed by 2000 mg on Cycle 1 Days 8, 15, and 22; Cycle 2 Days 1, 8, 15, and 22; followed 5 weeks later on Day 1 of Cycles 4-12.

Number of subjects in period 1	Dinaciclib	Ofatumumab
Started	20	24
Treated	20	22
Completed	10	10
Not completed	10	14
Physician decision	1	1
Adverse event, non-fatal	3	1
Death	1	5
Progressive Disease	4	4
Unknown	-	1
Study terminated by sponsor	-	1
Subject left study; reason related to study drug	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Dinaciclib
Reporting group description:	
Participants received dinaciclib, administered intravenously, over 2 hours at a dose of 7 mg/m^2 on Day 1, 10 mg/m^2 on Day 8, and 14 mg/m^2 on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m^2 on Days 1, 8, and 15 of each 28-day cycle for a total of 12 cycles.	
Reporting group title	Ofatumumab
Reporting group description:	
Participants received ofatumumab, administered intravenously, at a dose of 300 mg on Cycle 1 Day 1, followed by 2000 mg on Cycle 1 Days 8, 15, and 22; Cycle 2 Days 1, 8, 15, and 22; followed 5 weeks later on Day 1 of Cycles 4-12.	

Reporting group values	Dinaciclib	Ofatumumab	Total
Number of subjects	20	24	44
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	60.1	62.5	
standard deviation	± 8.6	± 8.7	-
Gender Categorical			
Units: Subjects			
Female	5	6	11
Male	15	18	33

End points

End points reporting groups

Reporting group title	Dinaciclib

Reporting group description:

Participants received dinaciclib, administered intravenously, over 2 hours at a dose of 7 mg/m^2 on Day 1, 10 mg/m^2 on Day 8, and 14 mg/m^2 on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m^2 on Days 1, 8, and 15 of each 28-day cycle for a total of 12 cycles.

Reporting group title	Ofatumumab

Reporting group description:

Participants received ofatumumab, administered intravenously, at a dose of 300 mg on Cycle 1 Day 1, followed by 2000 mg on Cycle 1 Days 8, 15, and 22; Cycle 2 Days 1, 8, 15, and 22; followed 5 weeks later on Day 1 of Cycles 4-12.

Primary: Median Progression-Free Survival (PFS)

End point title	Median Progression-Free Survival (PFS)[1]

End point description:

Median PFS was defined as the time from randomization to disease progression, or death, whichever occurred first, and was based on investigator's assessment. This endpoint was based on the Intent to Treat (ITT) population, defined as all randomized participants.

End point type	Primary

End point timeframe:

Up to approximately 38 months

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: No formal between-group statistical analysis was conducted for the primary end point Median Progression-Free Survival (PFS).

End point values	Dinaciclib	Ofatumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	24		
Units: Weeks				
median (confidence interval 95%)	59.7 (45 to 92.1)	25.7 (9.3 to 40.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (OR)

End point title	Best Overall Response (OR)

End point description:

Responses were based on investigator's best assessment across time points, according to 2008 iwCLL criteria. Types of overall response could be: Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Non-evaluable (NE) or No Assessment. This endpoint was based on the ITT population, defined as all randomized participants.

End point type	Secondary

End point timeframe:

Up to approximately 38 months

End point values	Dinaciclib	Ofatumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	24		
Units: Number of Participants				
Complete Response (CR)	0	0		
Partial Response (PR)	8	2		
Overall Response (CR + PR)	8	2		
Stable Disease (SD)	7	11		
Disease Control (CR + PR + SD)	15	13		
Progressive Disease (PD)	1	1		
Non-evaluable (NE)	1	2		
No Assessment	3	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Median Overall Survival

End point title	Median Overall Survival

End point description:

Overall survival was calculated from the date of randomization until the date of death. (Note regarding dinaciclib treatment group Confidence Interval, 99999: Upper limit was not reached at the time of analysis.)

End point type	Secondary

End point timeframe:

Up to approximately 38 months

End point values	Dinaciclib	Ofatumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	24		
Units: Months				
median (confidence interval 95%)	21.2 (16.6 to 99999)	16.7 (2.3 to 20.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 39 months

Adverse event reporting additional description:

The safety analysis was based on the All Patients as Treated (APaT) population, which consisted of all randomized participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Dinaciclib

Reporting group description:

Participants received dinaciclib, administered intravenously, over 2 hours at a dose of 7 mg/m^2 on Day 1, 10 mg/m^2 on Day 8, and 14 mg/m^2 on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m^2 on Days 1, 8, and 15 of each 28-day cycle for a total of 12 cycles.

Reporting group title	Ofatumumab

Reporting group description:

Participants received ofatumumab, administered intravenously, at a dose of 300 mg on Cycle 1 Day 1, followed by 2000 mg on Cycle 1 Days 8, 15, and 22; Cycle 2 Days 1, 8, 15, and 22; followed 5 weeks later on Day 1 of Cycles 4-12.

Serious adverse events	Dinaciclib	Ofatumumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	11 / 22 (50.00%)	
number of deaths (all causes)	5	6	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm progression			
subjects affected / exposed	1 / 20 (5.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutropenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Bone pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (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	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site cellulitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			

subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)	3 / 22 (13.64%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	1 / 1	0 / 3	
Sepsis			
subjects affected / exposed	1 / 20 (5.00%)	3 / 22 (13.64%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 3	
Septic shock			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dinaciclib	Ofatumumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 20 (80.00%)	14 / 22 (63.64%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 20 (10.00%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Neutrophil count decreased			
subjects affected / exposed	4 / 20 (20.00%)	2 / 22 (9.09%)	
occurrences (all)	8	2	
Aspartate aminotransferase increased			

subjects affected / exposed	2 / 20 (10.00%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 20 (25.00%)	0 / 22 (0.00%)	
occurrences (all)	6	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	7 / 20 (35.00%)	2 / 22 (9.09%)	
occurrences (all)	33	9	
Anemia			
subjects affected / exposed	3 / 20 (15.00%)	3 / 22 (13.64%)	
occurrences (all)	11	13	
Thrombocytopaenia			
subjects affected / exposed	4 / 20 (20.00%)	2 / 22 (9.09%)	
occurrences (all)	13	9	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 20 (20.00%)	2 / 22 (9.09%)	
occurrences (all)	5	2	
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	3 / 20 (15.00%)	2 / 22 (9.09%)	
occurrences (all)	3	2	
Chills			
subjects affected / exposed	1 / 20 (5.00%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Oedema peripheral			
subjects affected / exposed	4 / 20 (20.00%)	2 / 22 (9.09%)	
occurrences (all)	6	2	
Pyrexia			
subjects affected / exposed	5 / 20 (25.00%)	3 / 22 (13.64%)	
occurrences (all)	8	4	
Gastrointestinal disorders			

Constipation			
subjects affected / exposed	4 / 20 (20.00%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
Abdominal distension			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)	2 / 22 (9.09%)	
occurrences (all)	6	2	
Mouth ulceration			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	7 / 20 (35.00%)	2 / 22 (9.09%)	
occurrences (all)	10	2	
Vomiting			
subjects affected / exposed	3 / 20 (15.00%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 20 (20.00%)	2 / 22 (9.09%)	
occurrences (all)	7	3	
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Productive cough			
subjects affected / exposed	3 / 20 (15.00%)	1 / 22 (4.55%)	
occurrences (all)	6	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)	1 / 22 (4.55%)	
occurrences (all)	2	2	
Rash			
subjects affected / exposed	0 / 20 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	4	
Skin lesion			

subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 20 (10.00%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
Muscle spasms			
subjects affected / exposed	3 / 20 (15.00%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	3 / 22 (13.64%)	
occurrences (all)	0	5	
Respiratory tract infection			
subjects affected / exposed	0 / 20 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2012	Amendment 1: The primary reason for this amendment was to clarify, in the Trial Procedures section, that uric acid and magnesium were to be included in the chemistry panel for further safety evaluation.
02 August 2012	Amendment 2: The primary reason for this amendment was the addition of a safety assessment requiring participants who met the definition of increased risk of drug-induced tumor lysis syndrome (TLS) to be treated with a short-term steroid-based regimen prior to randomizing to either dinaciclib or ofatumumab. This required the screening period for such participants to be extended up to 35 days and adverse event (AE) monitoring was to begin immediately with initiation of steroid treatment. Furthermore, an additional stratification factor was added based on a participant’s increased or standard risk of TLS.
19 August 2013	Amendment 3: The primary reason for this amendment was to state that enrollment in this protocol had been prematurely discontinued due to program prioritization and was not related to any safety concerns. Participant randomization ended on September 9, 2013. Participants who were enrolled in the study and who had not yet met established protocol discontinuation criteria were able continue to receive study therapy per protocol and be seen by the investigator per usual standard of care, provided the investigator felt such treatment was in the participant's best interest.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported