



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/m² on Day 1, 10 mg/m² on Day 8, and 14 mg/m² on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m² 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/m² on Day 1, 10 mg/m² on Day 8, and 14 mg/m² on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m² 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/m² on Day 1, 10 mg/m² on Day 8, and 14 mg/m² on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m² 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 standard deviation | 60.1 ± 8.6 | 62.5 ± 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/m² on Day 1, 10 mg/m² on Day 8, and 14 mg/m² on Day 15 in Cycle 1. Starting in Cycle 2 and thereafter, dinaciclib was administered at a dose of 14 mg/m² 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 | |
| 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 | |
| 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 | |
| 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 occurrences (all) | 2 / 20 (10.00%) 4 | 1 / 22 (4.55%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 5 / 20 (25.00%) 6 | 0 / 22 (0.00%) 0 | |
| Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Anemia subjects affected / exposed occurrences (all) Thrombocytopaenia subjects affected / exposed occurrences (all) | 7 / 20 (35.00%) 33 3 / 20 (15.00%) 11 4 / 20 (20.00%) 13 | 2 / 22 (9.09%) 9 3 / 22 (13.64%) 13 2 / 22 (9.09%) 9 | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 4 / 20 (20.00%) 5 0 / 20 (0.00%) 0 3 / 20 (15.00%) 3 1 / 20 (5.00%) 1 4 / 20 (20.00%) 6 5 / 20 (25.00%) 8 | 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2 2 / 22 (9.09%) 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 occurrences (all) | 2 / 20 (10.00%) 2 | 0 / 22 (0.00%) 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