# Clinical trial results:
# A Phase 2, Open-Label, Multicenter, Dose-Escalation and Expansion Study of Venetoclax in Combination with Pomalidomide and Dexamethasone in Subjects with Relapsed or Refractory Multiple Myeloma

## Summary

| | |
|---|---|
| EudraCT number | 2017-004232-11 |
| Trial protocol | ES |
| Global end of trial date | 24 June 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 25 June 2021 |
| First version publication date | 25 June 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | M16-085 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03567616 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | AbbVie |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |
| Scientific contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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 | 24 June 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 June 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

This was an open-label, multicenter study designed to evaluate the safety and preliminary efficacy of venetoclax combined with pomalidomide and dexamethasone in subjects with relapsed or refractory (R/R) multiple myeloma (MM) who received at least 1 prior line of therapy with documented evidence of progression during or after the last treatment regimen. The study was designed to have 2 parts: Part 1 (dose escalation) and Part 2 (dose expansion). Part 2 subjects were to be divided into 2 cohorts, those positive and negative for t(11;14) translocation. After primary progression-free survival (PFS) analysis of EudraCT 2015-004411-20, MM studies were placed on partial clinical hold (PCH) by US FDA. Sponsor did not pursue PCH release for this study; subjects in Part 1 deriving clinical benefit were allowed to continue to receive treatment until disease progression. The study was discontinued when the last participant completed study treatment. No participants were enrolled in Part 2.

Protection of trial subjects:

Subjects must have voluntarily signed and dated an informed consent, approved by an Independent Ethics Committee (IEC)/Institutional Review Board (IRB), before the initiation of any screening or study-specific procedures.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 18 October 2018 |
| 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 | United States: 6 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Worldwide total number of subjects | 8 |
| EEA total number of subjects | 1 |

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) | 2 |
| From 65 to 84 years | 6 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Full Analysis Set: participants who received at least 1 dose of study drug

### Period 1

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

### Arms

| | |
|---|---|
| **Arm title** | All Participants |

Arm description:

Participants who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Venetoclax |
| Investigational medicinal product code | |
| Other name | ABT-199, GDC-0199, Venclexta |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400 mg oral [PO], once daily [QD]

| | |
|---|---|
| Investigational medicinal product name | Pomalidomide |
| Investigational medicinal product code | |
| Other name | Pomalyst |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

4 mg oral [PO], once daily [QD]

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

Dosage and administration details:

40 mg once weekly [qw]. For participants over 75 years of age, dexamethasone could have been administered at a 20 mg dose [qw]

| **Number of subjects in period 1** | All Participants |
|---|---|
| Started | 8 |
| Completed | 0 |
| Not completed | 8 |
| Death | 1 |
| Physician decision | 1 |
| Withdrawal by subject | 1 |
| Adverse event, non-fatal | 1 |
| Disease progression | 4 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall Study |
|---|---|

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|---|---|---|---|
| Number of subjects | 8 | 8 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>median<br>full range (min-max) | <br><br>67.5<br>60 to 77 | <br><br><br>- | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 5 | 5 | |
| Male | 3 | 3 | |

### Subject analysis sets

| Subject analysis set title | Participants Positive for t(11;14) Translocation |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants positive for t(11;14) translocation who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| Subject analysis set title | Participants Negative for t(11;14) Translocation |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants negative for t(11;14) translocation who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| Reporting group values | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|
| Number of subjects | 3 | 5 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: years<br>median<br>full range (min-max) | <br><br>68.0<br>67 to 74 | <br><br>66.0<br>60 to 77 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 1 | 4 | |
| Male | 2 | 1 | |

## End points

### End points reporting groups

| Reporting group title | All Participants |
|---|---|

Reporting group description:

Participants who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| Subject analysis set title | Participants Positive for t(11;14) Translocation |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants positive for t(11;14) translocation who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| Subject analysis set title | Participants Negative for t(11;14) Translocation |
|---|---|
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants negative for t(11;14) translocation who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

### Primary: Overall Response Rate (ORR)

| End point title | Overall Response Rate (ORR)[1] |
|---|---|

End point description:

ORR is defined as the percentage of participants experiencing a stringent complete response (sCR), complete response (CR), very good partial response (VGPR), or partial response (PR) using the International Myeloma Working Group (IMWG) 2016 criteria for disease response and progression. CR= negative immunofixation of serum and urine and disappearance of any soft tissue plasmacytomas, and < 5% plasma cells in bone marrow; sCR= CR + normal serum free light chain (FLC) ratio and absence of clonal cells in bone marrow; VGPR= serum and urine M-protein detectable by immunofixation but not on electrophoresis or ≥ 90% reduction in serum M-protein level + urine M-protein level < 100 mg per 24 hours; PR= ≥ 50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg per 24 hours.

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

End point timeframe:

Approximately 15 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: This was a dose escalation and expansion single arm trial, with the primary focus on safety. Efficacy endpoints were of lesser priority, with no preplanned statistical analyses.

| **End point values** | All Participants | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 8[2] | 3[3] | 5[4] | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 62.5 (24.5 to 91.5) | 66.7 (9.4 to 99.2) | 60.0 (14.7 to 94.7) | |

Notes:

[2] - Full Analysis Set: participants who received at least 1 dose of study drug

[3] - Full Analysis Set: participants who received at least 1 dose of study drug

[4] - Full Analysis Set: participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Adverse Events

| End point title | Number of Participants With Adverse Events[5] |
|---|---|

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either reasonable possibility or no reasonable possibility. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the participant and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs/TESAEs) are defined as any event that began or worsened in severity after the first dose of study drug. For more details on adverse events please see the Adverse Event section.

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

End point timeframe:

From first dose of study drug until 30 days following last dose of study drug (up to 70 weeks)

Notes:

[5] - 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: Descriptive data are summarized for this endpoint per protocol

| **End point values** | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 3[6] | 5[7] | | |
| Units: participants | | | | |
| Any TEAE | 3 | 5 | | |
| TESAE | 3 | 2 | | |

Notes:

[6] - Safety Analysis Set: participants who received at least 1 dose of study drug

[7] - Safety Analysis Set: participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time-to-progression (TTP)

| End point title | Time-to-progression (TTP) |
|---|---|

End point description:

TTP for a given participant is defined as the number of days from the date of first dose to the date of first documented disease progression (PD) or death due to multiple myeloma (MM), whichever occurs first. If the participant did not have an event of PD and the participant had not died due to MM, the participant's data was to be censored.

00000 and 99999 in the table below indicate values that are not calculable/estimable due to low number of participants with events.

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

End point timeframe:

Approximately 15 months

| End point values | All Participants | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 8[8] | 3[9] | 5[10] | |
| Units: days | | | | |
| median (confidence interval 95%) | 420.0 (57.0 to 99999) | 420.0 (00000 to 99999) | 99999 (57.0 to 99999) | |

Notes:

[8] - FAS: subjects rcvd ≥1 dose of study drug + had disease progression or death due to multiple myeloma
[9] - FAS: subjects rcvd ≥1 dose of study drug + had disease progression or death due to multiple myeloma
[10] - FAS: subjects rcvd ≥1 dose of study drug + had disease progression or death due to multiple myeloma

### Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS)

| End point title | Progression-Free Survival (PFS) |
|---|---|

End point description:

PFS is defined as the number of days from the date of first dose of any study drug to the date of disease progression or death, whichever occurs first. All disease progression was to be included regardless of whether the event occurred during or after the participant was taking any study drug.

99999 in the table below indicates values that are not calculable/estimable due to low number of participants with events.

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

End point timeframe:

Approximately 20 months

| End point values | All Participants | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 8[11] | 3[12] | 5[13] | |
| Units: days | | | | |
| median (confidence interval 95%) | 320.0 (11.0 to 99999) | 220.0 (11.0 to 99999) | 99999 (57.0 to 99999) | |

Notes:

[11] - Full Analysis Set: participants who received at least 1 dose of study drug

[12] - Full Analysis Set: participants who received at least 1 dose of study drug

[13] - Full Analysis Set: participants who received at least 1 dose of study drug

### Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR)

| End point title | Duration of Response (DOR) |
|---|---|

End point description:

DOR for a given participant is defined as the number of days from the date of that participant's first documented response (Partial Response [PR] or better) to the date of first documented disease progression (PD) or death due to multiple myeloma (MM), whichever occurs first. If the participant with a documented response did not have an event of PD and the participant had not died due to MM, the participant's data was to be censored.

00000 and 99999 in the table below indicate values that are not calculable/estimable due to low number of participants with events.

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

End point timeframe:

Approximately 15 months

| **End point values** | All Participants | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 5[14] | 2[15] | 3[16] | |
| Units: days | | | | |
| median (confidence interval 95%) | 393.0 (00000 to 99999) | 393.0 (00000 to 99999) | 00000 (00000 to 99999) | |

Notes:

[14] - FAS: subjects rcvd ≥1 dose of study drug + had disease progression or death due to multiple myeloma

[15] - FAS: subjects rcvd ≥1 dose of study drug + had disease progression or death due to multiple myeloma

[16] - FAS: subjects rcvd ≥1 dose of study drug + had disease progression or death due to multiple myeloma

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from the first dose of study drug until 30 days after last study drug administration, up to 70 weeks.

Adverse event reporting additional description:

TEAEs and SAEs are defined as any AE or SAE with onset or worsening reported by a participant from the time that the first dose of study drug is administered until 30 days have elapsed following discontinuation of study drug. TEAEs were collected whether elicited or spontaneously reported by the participant.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Participants Positive for t(11;14) Translocation |

Reporting group description:

Participants positive for t(11;14) translocation who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| | |
|---|---|
| Reporting group title | Participants Negative for t(11;14) Translocation |

Reporting group description:

Participants negative for t(11;14) translocation who received at least 1 dose of study drug (venetoclax 400 mg, pomalidomide 4 mg, and dexamethasone 40 mg)

| Serious adverse events | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 2 / 5 (40.00%) | |
| number of deaths (all causes) | 2 | 0 | |
| number of deaths resulting from adverse events | 2 | 0 | |
| Investigations | | | |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| PANCREATIC NEOPLASM | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| CEREBRAL INFARCTION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Infections and infestations | | | |
| PNEUMOCOCCAL INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA STREPTOCOCCAL | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 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** | Participants Positive for t(11;14) Translocation | Participants Negative for t(11;14) Translocation | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 5 / 5 (100.00%) | |
| Vascular disorders | | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 2 | 2 | |
| HYPOTENSION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 2 | |
| General disorders and administration site conditions | | | |
| FATIGUE | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 2 / 5 (40.00%) | |
| occurrences (all) | 3 | 3 | |
| CHILLS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| INSOMNIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |

| | | | |
|---|---|---|---|
| Reproductive system and breast disorders | | | |
| VULVOVAGINAL PRURITUS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 2 | 1 | |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| BLOOD IMMUNOGLOBULIN G DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 5 | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 5 | |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 5 (40.00%) | |

| | | | |
|---|---|---|---|
| occurrences (all) | 0 | 15 | |

| | | | |
|---|---|---|---|
| Cardiac disorders | | | |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 5 (60.00%) | |
| occurrences (all) | 1 | 4 | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 5 (40.00%) | |
| occurrences (all) | 3 | 14 | |
| NEUTROPENIA | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 4 / 5 (80.00%) | |
| occurrences (all) | 10 | 34 | |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 6 | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 5 (40.00%) | |
| occurrences (all) | 1 | 6 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| DYSPHONIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| DYSPNOEA | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 5 (20.00%) | |
| occurrences (all) | 3 | 1 | |
| DYSPNOEA EXERTIONAL | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| NASAL CONGESTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 0 / 5 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| RESPIRATORY ACIDOSIS | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| APHASIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| DISTURBANCE IN ATTENTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| DYSGEUSIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| PARAESTHESIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 2 | |
| TREMOR | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| CONSTIPATION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |

| | | | |
|---|---|---|---|
| occurrences (all) | 0 | 2 | |
| FLATULENCE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| NAUSEA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 2 | |
| VOMITING | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| TOOTHACHE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| HYPERBILIRUBINAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Skin and subcutaneous tissue disorders | | | |
| ERYTHEMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| RASH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| BONE PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |

| | | | |
|---|---|---|---|
| occurrences (all) | 0 | 1 | |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| NECK PAIN | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 5 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 5 (60.00%) | |
| occurrences (all) | 0 | 3 | |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| HYPERURICAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 5 (40.00%) | |
| occurrences (all) | 0 | 2 | |
| HYPOALBUMINAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| HYPOGLYCAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| HYPOKALAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 5 (60.00%) | |
| occurrences (all) | 1 | 5 | |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 5 (20.00%) | |
| occurrences (all) | 1 | 1 | |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 5 (40.00%) | |
| occurrences (all) | 1 | 2 | |
| Infections and infestations | | | |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 3 | |
| VULVOVAGINAL MYCOTIC INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 5 (20.00%) | |
| occurrences (all) | 0 | 1 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 June 2018 | Version 2.0<br>• Included recent data from a study of venetoclax in combination with a proteasome inhibitor (Study M14-031, Bellini study) where a higher proportion of deaths possibly related to infections was observed in the venetoclax arm<br>• Updated eligibility Criterion 14 (Section 5.1) and the synopsis (Section 1)<br>• Modified Section 5.4 to provide guidance on vaccinations while on study<br>• Modified Section 6.4 to strongly recommend consideration of G-CSF<br>• Modified Section 6.4 (Management of Infections) to strongly recommend close monitoring of infections during subject study participation including treatment modification recommendations<br>• Modified Table 10 (Toxicities Related to Venetoclax) to keep consistency with modifications mentioned above |
| 15 March 2019 | Version 3.0<br>• Updated Section 4.1 to modify dosing instructions |
| 02 October 2019 | Version 4.0<br>• Clarified allowable corticosteroid use while on study treatment<br>• Based on BELLINI interim analysis, recommendations provided for the use of and the timing for prophylactic antibiotics; in addition, recommendations provided for the administration of intravenous immunoglobulin (IVIG)<br>• Provided further guidance on vaccinations and to align with recommendations set forth by the National Comprehensive Cancer Network (NCCN) and the Center for Disease Control (CDC) in patients with multiple myeloma<br>• Provided further guidance for tumor lysis syndrome (TLS) prophylaxis<br>• Provided instruction for dispensing of pomalidomide<br>• Provided AEs of special interest<br>• Referenced a Safety Review Committee (SRC) separate from the study team that will provide regular review of safety data<br>• Included progression-free survival follow-up visits<br>• Included survival follow-up assessments |
| 24 June 2020 | Version 5.0<br>• Updated pneumococcal and influenza vaccination requirements<br>• Updated the list of signatories in Appendix C per current standard operating procedure<br>• Deleted the progression-free survival follow-up visits<br>• Deleted the survival follow-up assessments |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported