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	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 6
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
Physician decision	1
Disease progression	4
Adverse event, non-fatal	1
Death	1
Withdrawal by subject	1

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 Units: Subjects			
Age continuous Units: years median full range (min-max)	 67.5 60 to 77	 -	
Gender categorical 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 Units: Subjects			
Age continuous Units: years median full range (min-max)	 68.0 67 to 74	 66.0 60 to 77	
Gender categorical 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: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events[1]

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:

[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: 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[2]	5[3]		
Units: participants				
Any TEAE	3	5		
TESAE	3	2		

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[4]

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:

[4] - 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[5]	3[6]	5[7]	
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:

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

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

[7] - 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[8]	2[9]	3[10]	
Units: days				
median (confidence interval 95%)	393.0 (00000 to 99999)	393.0 (00000 to 99999)	00000 (00000 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: 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[11]	3[12]	5[13]	
Units: days				
median (confidence interval 95%)	420.0 (57.0 to 99999)	420.0 (00000 to 99999)	99999 (57.0 to 99999)	

Notes:

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

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[14]	3[15]	5[16]	
Units: days				
median (confidence interval 95%)	320.0 (11.0 to 99999)	220.0 (11.0 to 99999)	99999 (57.0 to 99999)	

Notes:

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

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

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

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	
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	
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	
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	
Reproductive system and breast disorders			
VULVOVAGINAL PRURITUS			
subjects affected / exposed	0 / 3 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
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	
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	
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	
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	
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	
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	
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	
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	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 June 2018	Version 2.0 • 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 • Updated eligibility Criterion 14 (Section 5.1) and the synopsis (Section 1) • Modified Section 5.4 to provide guidance on vaccinations while on study • Modified Section 6.4 to strongly recommend consideration of G-CSF • Modified Section 6.4 (Management of Infections) to strongly recommend close monitoring of infections during subject study participation including treatment modification recommendations • Modified Table 10 (Toxicities Related to Venetoclax) to keep consistency with modifications mentioned above
15 March 2019	Version 3.0 • Updated Section 4.1 to modify dosing instructions
02 October 2019	Version 4.0 • Clarified allowable corticosteroid use while on study treatment • 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) • 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 • Provided further guidance for tumor lysis syndrome (TLS) prophylaxis • Provided instruction for dispensing of pomalidomide • Provided AEs of special interest • Referenced a Safety Review Committee (SRC) separate from the study team that will provide regular review of safety data • Included progression-free survival follow-up visits • Included survival follow-up assessments
24 June 2020	Version 5.0 • Updated pneumococcal and influenza vaccination requirements • Updated the list of signatories in Appendix C per current standard operating procedure • Deleted the progression-free survival follow-up visits • Deleted the survival follow-up assessments

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported