Clinical trial results:
A Phase 2, Multicenter, Open-label, Study to Determine the Safety and Efficacy for the Combination of Durvalumab (DURVA) and Daratumumab (DARA) (D2) in Subjects With Relapsed and Refractory Multiple Myeloma (RRMM) (FUSION MM-003)

Summary

EudraCT number	2016-001209-17
Trial protocol	DE SE DK ES BE GB IT
Global end of trial date	03 January 2022

Results information

Result version number	v1 (current)
This version publication date	20 January 2023
First version publication date	20 January 2023

Trial information

Trial identification

Sponsor protocol code	MEDI4736-MM-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02807454
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	30 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 January 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and efficacy for the combination of Durvalumab (DURVA) and Daratumumab (DARA) (D2) in participants with relapsed and refractory multiple myeloma (RRMM).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 July 2016
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	Canada: 5
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	37
EEA total number of subjects	19

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)	19
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive either Durvalumab + Daratumumab (D2) or Durvalumab + Daratumumab + Pomalidomide + Dexamethasone (PD3). 32 participants were treated in the Simon Stage 1: D2 arm. No participants enrolled in the Simon Stage 2: D2 arm. 5 participants treated in the PD3 arm.

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	Simon Stage 1: D2 Arm

Arm description:

Durvalumab 1500 mg + Daratumumab 16 mg/kg were administered intravenously within a 28-day cycle for a maximum of 60 cycles. POM + DEX could be added to the D2 regimen, at the investigator's discretion, upon confirmed progressive disease for participants who had at least 2 cycles of D2.

Arm type	Experimental
Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Daratumumab 16 mg/kg administered intravenously within a 28-day cycle for a maximum of 60 cycles

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg administered intravenously within a 28-day cycle for a maximum of 60 cycles

Arm title	PD3 Arm

Arm description:

Durvalumab 1500 mg IV + Daratumumab 16 mg/kg IV + Pomalidomide 4 mg/day Oral + Dexamethasone 40 mg Oral (20 mg for > 75 Years Old) administered within a 28-day cycle for a maximum of 22 cycles

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg administered intravenously within a 28-day cycle for a maximum of 22 cycles

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

Dosage and administration details:

Pomalidomide 4 mb/day administered orally within a 28-day cycle for a maximum of 22 cycles

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

Dosage and administration details:

Dexamethasone 40 mg (20 mg for > 75 Years Old) administered orally within a 28-day cycle for a maximum of 22 cycles

Investigational medicinal product name	Daratumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Daratumumab 16 mg/kg administered intravenously within a 28-day cycle for a maximum of 22 cycles

Number of subjects in period 1	Simon Stage 1: D2 Arm	PD3 Arm
Started	32	5
D2 participants who received POM+DEX	7	0
Completed	0	0
Not completed	32	5
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-
Other Reasons	1	1
Progressive Disease	30	3

Baseline characteristics

Reporting groups	
Reporting group title	Simon Stage 1: D2 Arm
Reporting group description:	
Durvalumab 1500 mg + Daratumumab 16 mg/kg were administered intravenously within a 28-day cycle for a maximum of 60 cycles. POM + DEX could be added to the D2 regimen, at the investigator's discretion, upon confirmed progressive disease for participants who had at least 2 cycles of D2.	
Reporting group title	PD3 Arm
Reporting group description:	
Durvalumab 1500 mg IV + Daratumumab 16 mg/kg IV + Pomalidomide 4 mg/day Oral + Dexamethasone 40 mg Oral (20 mg for > 75 Years Old) administered within a 28-day cycle for a maximum of 22 cycles	

Reporting group values	Simon Stage 1: D2 Arm	PD3 Arm	Total
Number of subjects	32	5	37
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	2	19
From 65-84 years	15	3	18
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	63.2	63	
standard deviation	± 7.58	± 5.66	-
Sex: Female, Male Units: Participants			
Female	13	1	14
Male	19	4	23
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	32	5	37
Unknown or Not Reported	0	0	0
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	31	5	36
Other	1	0	1

Subject analysis sets

Subject analysis set title	Simon Stage 1: D2 + Pomalidomide + Dexamethasone
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Durvalumab 1500 mg IV + Daratumumab 16 mg/kg IV + Pomalidomide 4 mg/day Oral + Dexamethasone 40 mg Oral (20 mg for > 75 Years Old) were administered within a 28-day cycle for a maximum of 60 cycles

Reporting group values	Simon Stage 1: D2 + Pomalidomide + Dexamethasone		
Number of subjects	7		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	4		
From 65-84 years	3		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean	63.4		
standard deviation	± 8.26		
Sex: Female, Male Units: Participants			
Female	4		
Male	3		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	7		
Unknown or Not Reported	0		
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	7		
Other	0		

End points

End points reporting groups

Reporting group title	Simon Stage 1: D2 Arm

Reporting group description:

Durvalumab 1500 mg + Daratumumab 16 mg/kg were administered intravenously within a 28-day cycle for a maximum of 60 cycles. POM + DEX could be added to the D2 regimen, at the investigator's discretion, upon confirmed progressive disease for participants who had at least 2 cycles of D2.

Reporting group title	PD3 Arm

Reporting group description:

Durvalumab 1500 mg IV + Daratumumab 16 mg/kg IV + Pomalidomide 4 mg/day Oral + Dexamethasone 40 mg Oral (20 mg for > 75 Years Old) administered within a 28-day cycle for a maximum of 22 cycles

Subject analysis set title	Simon Stage 1: D2 + Pomalidomide + Dexamethasone
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Durvalumab 1500 mg IV + Daratumumab 16 mg/kg IV + Pomalidomide 4 mg/day Oral + Dexamethasone 40 mg Oral (20 mg for > 75 Years Old) were administered within a 28-day cycle for a maximum of 60 cycles

Primary: Overall Response Rate (ORR)

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

End point description:

Tumor response of partial response (PR) or better was assessed using the International Myeloma Working Group (IMWG) Uniform Response Criteria. ORR was calculated as the percent of responders (multiplied by 100). Partial response required ≥ 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:

From first dose to up to approximately 66 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: Only summary statistics planned for this endpoint.

End point values	Simon Stage 1: D2 Arm	PD3 Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	4		
Units: Percentage of participants				
number (not applicable)	53.1	75.0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[2]

End point description:

Number of participants who experienced at least one adverse event. An adverse event (AE) is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury,

or any concomitant impairment of the participant’s health, including laboratory test values, regardless of etiology. Any worsening (ie, any clinically significant adverse change in the frequency or intensity of a preexisting condition should be considered an AE.

End point type	Primary

End point timeframe:

From first dose to 90 days after last dose (up to approximately 58 months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint.

End point values	Simon Stage 1: D2 Arm	PD3 Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	5		
Units: Participants	31	5		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Serious Adverse Events (SAEs)

End point title	Number of Participants with Serious Adverse Events (SAEs)[3]

End point description:

Number of participants who experienced at least one serious adverse event. An SAE is any AE occurring at any dose that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, constitutes an important medical event.

End point type	Primary

End point timeframe:

From first dose to 90 days after last dose (up to approximately 58 months)

Notes:

[3] - 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: Only summary statistics planned for this endpoint.

End point values	Simon Stage 1: D2 Arm	PD3 Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	5		
Units: Participants	17	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Time-To-Response (TTR)

End point title	Time-To-Response (TTR)

End point description:

Time-to-response is calculated as the time from enrollment to the first date of documented response (partial response or better). Tumor response of partial response (PR) or better was assessed using the International Myeloma Working Group (IMWG) Uniform Response Criteria. Partial response required ≥ 50% reduction of serum M-Protein and reduction in 24-hour urinary M protein by ≥ 90% or to < 200 mg per 24 hours. For those participants where POM + DEX were added, time-to-response was calculated from the date POM and DEX were added to the first date of documented response (PR or better).

End point type	Secondary

End point timeframe:

From enrollment to earliest documented response (up to approximately 66 months)

End point values	Simon Stage 1: D2 Arm	PD3 Arm	Simon Stage 1: D2 + Pomalidomide + Dexamethasone	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	32	4	7	
Units: Weeks				
median (full range (min-max))	4.29 (4.0 to 12.0)	8.14 (4.3 to 8.3)	5.07 (4.1 to 8.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Duration of Response (DOR) - Simon Stage 1: D2 Arm

End point title	Kaplan-Meier Estimate of Duration of Response (DOR) - Simon Stage 1: D2 Arm[4]

End point description:

Duration of response was calculated as the time from the earliest date of documented response (PR or better) to the earliest date of disease progression as determined by the investigator. For those participants where POM + DEX was added, duration of response was calculated as the time from the earliest date of documented response after POM + DEX was added (PR or better) to the earliest date of disease. Tumor response of partial response (PR) or better was assessed using the International Myeloma Working Group (IMWG) Uniform Response Criteria. Partial response required ≥ 50% reduction of serum M-Protein and reduction in 24-hour urinary M protein by ≥ 90% or to < 200 mg per 24 hours. Progressive Disease required increase of 25% from lowest response value in the serum M-component (absolute increase must be ≥ 0.5 g/dL) and/or urine M-component (absolute increase must be ≥ 200 mg/24 h).

End point type	Secondary

End point timeframe:

From the earliest date of documented response (PR or better) to earliest date of progressive disease (up to approximately 66 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Simon Stage 1: D2 Arm	Simon Stage 1: D2 + Pomalidomide + Dexamethasone		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	32	7		
Units: Months				
median (confidence interval 95%)	8.31 (3.7 to 11.1)	8.41 (3.7 to 12.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Duration of Response (DOR) - PD3 Arm

End point title	Kaplan-Meier Estimate of Duration of Response (DOR) - PD3 Arm[5]

End point description:

Duration of response was calculated as the time from the earliest date of documented response (PR or better) to the earliest date of disease progression as determined by the investigator. For those participants where POM + DEX was added, duration of response was calculated as the time from the earliest date of documented response after POM + DEX was added (PR or better) to the earliest date of disease progression as determined by the investigator. Participants who are alive or lost to follow-up will be censored on the last-known-to-be-alive date. Tumor response of partial response (PR) or better was assessed using the International Myeloma Working Group (IMWG) Uniform Response Criteria. Partial response required ≥ 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	Secondary

End point timeframe:

From the earliest date of documented response (PR or better) to earliest date of progressive disease (up to approximately 66 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	PD3 Arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Months				
median (confidence interval 80%)	7.62 (6.7 to 17.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Progression-Free Survival (PFS) - Simon Stage 1: D2 Arm

End point title	Kaplan-Meier Estimate of Progression-Free Survival (PFS) -

	Simon Stage 1: D2 Arm[6]

End point description:

Progression-free survival was calculated as the time between the enrollment to the first documentation of progressive disease or death from any cause during study, whichever occurs earlier using the International Myeloma Working Group (IMWG) Uniform Response Criteria. Progressive Disease required increase of 25% from lowest response value in the serum M-component (absolute increase must be ≥ 0.5 g/dL) and/or urine M-component (absolute increase must be ≥ 200 mg/24 h).

End point type	Secondary

End point timeframe:

From enrollment to first documentation of progressive disease or death from any cause during study, whichever occurs earlier (up to approximately 66 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Simon Stage 1: D2 Arm	Simon Stage 1: D2 + Pomalidomide + Dexamethasone		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	32	7		
Units: Months				
median (confidence interval 95%)	5.74 (2.0 to 6.5)	8.05 (3.7 to 12.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of Progression-Free Survival (PFS) - PD3 Arm

End point title	Kaplan-Meier Estimate of Progression-Free Survival (PFS) - PD3 Arm[7]

End point description:

Progression-free survival was calculated as the time between the enrollment to the first documentation of progressive disease or death from any cause during study, whichever occurs earlier using the International Myeloma Working Group (IMWG) Uniform Response Criteria. Progressive Disease required increase of 25% from lowest response value in the serum M-component (absolute increase must be ≥ 0.5 g/dL) and/or urine M-component (absolute increase must be ≥ 200 mg/24 h).

End point type	Secondary

End point timeframe:

From enrollment to first documentation of progressive disease or death from any cause during study, whichever occurs earlier (up to approximately 66 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoints are cohort specific and do not report for all arms.

End point values	PD3 Arm			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Months				
median (confidence interval 80%)	9.02 (6.9 to 18.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) - Simon Stage 1: D2 Arm

End point title	Maximum Observed Plasma Concentration (Cmax) - Simon Stage 1: D2 Arm[8]

End point description:

Pharmacokinetics of Durvalumab derived from serum concentration versus time data.

End point type	Secondary

End point timeframe:

Cycle 1 - Days 2, 8, 15, 22

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Simon Stage 1: D2 Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: ug/mL				
geometric mean (geometric coefficient of variation)	315.806 (± 34.832)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Observed Concentration (Tmax) - Simon Stage 1: D2 Arm

End point title	Time of Maximum Observed Concentration (Tmax) - Simon Stage 1: D2 Arm[9]

End point description:

Pharmacokinetics of Durvalumab derived from serum concentration versus time data.

End point type	Secondary

End point timeframe:

Cycle 1 - Days 2, 8, 15, 22

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Simon Stage 1: D2 Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Hour				
median (full range (min-max))	1.150 (1.03 to 1.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve to the Last Measurable Plasma Concentration [AUC(0-Last)] - Simon Stage 1: D2 Arm

End point title	Area Under the Plasma Concentration-Time Curve to the Last Measurable Plasma Concentration [AUC(0-Last)] - Simon Stage 1: D2 Arm[10]

End point description:

Pharmacokinetics of Durvalumab derived from serum concentration versus time data.

End point type	Secondary

End point timeframe:

Cycle 1 - Days 2, 8, 15, 22

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Simon Stage 1: D2 Arm			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Hour*ug/mL				
geometric mean (geometric coefficient of variation)	77831.751 (± 48.535)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve in 1 Dosing Interval [AUC(TAU)] - Simon Stage 1: D2 Arm

End point title	Area Under the Plasma Concentration-Time Curve in 1 Dosing Interval [AUC(TAU)] - Simon Stage 1: D2 Arm[11]

End point description:

Pharmacokinetics of Durvalumab derived from serum concentration versus time data.

End point type	Secondary

End point timeframe:

Cycle 1 - Days 2, 8, 15, 22

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoints are cohort specific and do not report for all arms.

End point values	Simon Stage 1: D2 Arm			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Hour*ug/mL				
geometric mean (geometric coefficient of variation)	83966.099 (± 46.115)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was assessed from the participant's first dose to their study completion (up to approximately 66 months). SAEs and Other AEs were assessed from first dose to 90 days after last dose of study therapy (up to approximately 58 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Simon Stage 1: D2 Arm

Reporting group description:

Durvalumab 1500 mg + Daratumumab 16 mg/kg were administered intravenously within a 28-day cycle for a maximum of 60 cycles. POM + DEX could be added to the D2 regimen, at the investigator’s discretion, upon confirmed progressive disease for participants who had at least 2 cycles of D2.

Reporting group title	PD3 Arm

Reporting group description:

Durvalumab 1500 mg IV + Daratumumab 16 mg/kg IV + Pomalidomide 4 mg/day Oral + Dexamethasone 40 mg Oral (20 mg for > 75 Years Old) administered within a 28-day cycle for a maximum of 22 cycles

Serious adverse events	Simon Stage 1: D2 Arm	PD3 Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 32 (53.13%)	2 / 5 (40.00%)	
number of deaths (all causes)	11	4	
number of deaths resulting from adverse events			
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasmacytoma			

subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 32 (9.38%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 32 (3.13%)	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			
Cellulitis streptococcal			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corynebacterium infection			

subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	7 / 32 (21.88%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	2 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 5 (40.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			

subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 32 (3.13%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	1 / 32 (3.13%)	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	Simon Stage 1: D2 Arm	PD3 Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 32 (96.88%)	5 / 5 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hypotension			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Chills			
subjects affected / exposed	2 / 32 (6.25%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Fatigue			
subjects affected / exposed	4 / 32 (12.50%)	2 / 5 (40.00%)	
occurrences (all)	6	2	
Gait disturbance			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	4 / 32 (12.50%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Mucosal inflammation			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Oedema			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	3 / 32 (9.38%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Pyrexia			
subjects affected / exposed	9 / 32 (28.13%)	0 / 5 (0.00%)	
occurrences (all)	12	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Cough			

subjects affected / exposed	7 / 32 (21.88%)	2 / 5 (40.00%)	
occurrences (all)	9	3	
Dyspnoea			
subjects affected / exposed	4 / 32 (12.50%)	2 / 5 (40.00%)	
occurrences (all)	5	2	
Epistaxis			
subjects affected / exposed	3 / 32 (9.38%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Nasal congestion			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Oropharyngeal pain			
subjects affected / exposed	3 / 32 (9.38%)	1 / 5 (20.00%)	
occurrences (all)	8	1	
Productive cough			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Rhinorrhoea			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Stridor			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	5 / 32 (15.63%)	1 / 5 (20.00%)	
occurrences (all)	6	1	
Restlessness			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	

Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
International normalised ratio increased			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 32 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Platelet count decreased			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	3 / 32 (9.38%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Infusion related reaction			
subjects affected / exposed	8 / 32 (25.00%)	0 / 5 (0.00%)	
occurrences (all)	8	0	
Jaw fracture			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Tachycardia			

subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Headache			
subjects affected / exposed	4 / 32 (12.50%)	0 / 5 (0.00%)	
occurrences (all)	5	0	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 32 (12.50%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Sciatica			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Somnolence			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	16 / 32 (50.00%)	3 / 5 (60.00%)	
occurrences (all)	26	3	
Febrile neutropenia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Leukopenia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 5 (20.00%)	
occurrences (all)	6	7	
Lymphopenia			
subjects affected / exposed	8 / 32 (25.00%)	1 / 5 (20.00%)	
occurrences (all)	8	1	
Neutropenia			
subjects affected / exposed	15 / 32 (46.88%)	3 / 5 (60.00%)	
occurrences (all)	33	4	
Thrombocytopenia			

subjects affected / exposed	7 / 32 (21.88%)	2 / 5 (40.00%)	
occurrences (all)	8	2	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Conjunctival irritation			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Ophthalmic vein thrombosis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Anal incontinence			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	5 / 32 (15.63%)	0 / 5 (0.00%)	
occurrences (all)	5	0	
Diarrhoea			
subjects affected / exposed	9 / 32 (28.13%)	3 / 5 (60.00%)	
occurrences (all)	20	3	
Dry mouth			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Dyspepsia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Nausea			

subjects affected / exposed	8 / 32 (25.00%)	2 / 5 (40.00%)	
occurrences (all)	8	2	
Stomatitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	4 / 32 (12.50%)	1 / 5 (20.00%)	
occurrences (all)	6	1	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	4 / 32 (12.50%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Hyperhidrosis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Pruritus			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Skin ulcer			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Pollakiuria			

subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 32 (25.00%)	2 / 5 (40.00%)	
occurrences (all)	8	2	
Back pain			
subjects affected / exposed	7 / 32 (21.88%)	4 / 5 (80.00%)	
occurrences (all)	8	4	
Bone pain			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Groin pain			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain			
subjects affected / exposed	3 / 32 (9.38%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Myalgia			
subjects affected / exposed	5 / 32 (15.63%)	0 / 5 (0.00%)	
occurrences (all)	7	0	
Pain in extremity			
subjects affected / exposed	5 / 32 (15.63%)	1 / 5 (20.00%)	
occurrences (all)	6	1	
Pathological fracture			

subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Spinal pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Cellulitis			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Influenza			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	2 / 32 (6.25%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
Oral candidiasis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Pneumococcal infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	6 / 32 (18.75%)	2 / 5 (40.00%)	
occurrences (all)	8	5	
Sinusitis			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Skin infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

Upper respiratory tract infection			
subjects affected / exposed	3 / 32 (9.38%)	3 / 5 (60.00%)	
occurrences (all)	6	5	
Urinary tract infection			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	5	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 32 (9.38%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Fluid retention			
subjects affected / exposed	0 / 32 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	1 / 32 (3.13%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Hypertriglyceridaemia			
subjects affected / exposed	3 / 32 (9.38%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 5 (20.00%)	
occurrences (all)	4	1	
Hypomagnesaemia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Hyponatraemia			
subjects affected / exposed	2 / 32 (6.25%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Increased appetite			
subjects affected / exposed	0 / 32 (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? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study stopped enrolling participants on 05-Sep-2017 and terminated on 03-Jan-2022. This results disclosure report provides outputs from the Simon Stage 1: D2 and PD3 arms. Simon Stage 2: D2 did not enroll any participants.

Notes: