Clinical trial results:
A Randomized Open-Label Phase 1/2 Study of INCB001158 Combined With Subcutaneous (SC) Daratumumab, Compared to Daratumumab SC, in Participants With Relapsed or Refractory Multiple Myeloma

Summary

EudraCT number	2018-004076-35
Trial protocol	ES
Global end of trial date	05 April 2022

Results information

Result version number	v1 (current)
This version publication date	05 April 2023
First version publication date	05 April 2023

Trial information

Trial identification

Sponsor protocol code	INCB 01158-206

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte Corporation
Sponsor organisation address	1801 Augustine Cutoff Drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.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	05 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety and antitumor activity of INCB001158 in combination with daratumumab subcutaneous (SC), compared with daratumumab SC alone, in participants with relapsed or refractory multiple myeloma.

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study is being conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 September 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	15
EEA total number of subjects	10

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)	7
From 65 to 84 years	7
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted at 11 study centers in Germany, Spain, and the United States.

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	Phase 1: INCB001158 75 mg BID + daratumumab

Arm description:

In Phase 1, participants received oral INCB001158 75 milligrams (mg) twice daily (BID) in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Arm type	Experimental
Investigational medicinal product name	daratumumab SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg/mL daratumumab + 20 µg/mL rHuPH20 solution

Investigational medicinal product name	INCB001158
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg and 100 mg tablets

Arm title	Phase 1: INCB001158 100 mg BID + daratumumab

Arm description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Arm type	Experimental
Investigational medicinal product name	daratumumab SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg/mL daratumumab + 20 µg/mL rHuPH20 solution

Investigational medicinal product name	INCB001158
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg and 100 mg tablets

Arm title	Phase 2: INCB001158 100 mg BID + daratumumab

Arm description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Arm type	Experimental
Investigational medicinal product name	daratumumab SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg/mL daratumumab + 20 µg/mL rHuPH20 solution

Investigational medicinal product name	INCB001158
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg and 100 mg tablets

Arm title	Phase 2: daratumumab; cross over to INCB001158 + daratumumab

Arm description:

In Part 1 of Phase 2, participants received daratumumb 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2 (28-day cycles), once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. At the time of confirmed disease progression, participants crossed over to Part 2 of Phase 2 to receive oral INCB001158 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Arm type	Experimental
Investigational medicinal product name	daratumumab SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg/mL daratumumab + 20 µg/mL rHuPH20 solution

Investigational medicinal product name	INCB001158
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg and 100 mg tablets

Arm title	Phase 2: INCB001158; cross over to INCB001158 +

	daratumumab

Arm description:

In Part 1 of Phase 2, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1. At the time of confirmed disease progression, participants crossed over to Part 2 of Part 2 to receive oral INCB001158 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Arm type	Experimental
Investigational medicinal product name	daratumumab SC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 mg/mL daratumumab + 20 µg/mL rHuPH20 solution

Investigational medicinal product name	INCB001158
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg and 100 mg tablets

Number of subjects in period 1	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab	Phase 2: INCB001158 100 mg BID + daratumumab
Started	6	4	2
Completed	1	2	2
Not completed	5	2	0
Adverse event, serious fatal	5	2	-

Number of subjects in period 1	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab
Started	1	2
Completed	0	1
Not completed	1	1
Adverse event, serious fatal	1	1

Baseline characteristics

Reporting groups

Reporting group title	Phase 1: INCB001158 75 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 75 milligrams (mg) twice daily (BID) in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 1: INCB001158 100 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 2: INCB001158 100 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 2: daratumumab; cross over to INCB001158 + daratumumab

Reporting group description:

In Part 1 of Phase 2, participants received daratumumb 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2 (28-day cycles), once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. At the time of confirmed disease progression, participants crossed over to Part 2 of Phase 2 to receive oral INCB001158 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Reporting group title	Phase 2: INCB001158; cross over to INCB001158 + daratumumab

Reporting group description:

In Part 1 of Phase 2, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1. At the time of confirmed disease progression, participants crossed over to Part 2 of Part 2 to receive oral INCB001158 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Reporting group values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab	Phase 2: INCB001158 100 mg BID + daratumumab
Number of subjects	6	4	2
Age categorical Units: Subjects			
Adults (18-64 years)	3	2	1
From 65-84 years	3	2	1
85 years and over	0	0	0
Age Continuous			
100=To protect participant privacy, a mean age and standard deviation are not reported for a single participant.			
Units: years arithmetic mean	65.0	68.0	67.0

standard deviation	± 11.70	± 9.83	± 12.73

Sex: Female, Male Units: participants			
Female	2	2	1
Male	4	2	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	5	4	2
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	4	2
Unknown or Not Reported	0	0	0

Reporting group values	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab	Total
Number of subjects	1	2	15
Age categorical Units: Subjects			
Adults (18-64 years)	0	1	7
From 65-84 years	1	0	7
85 years and over	0	1	1
Age Continuous			
100=To protect participant privacy, a mean age and standard deviation are not reported for a single participant.			
Units: years			
arithmetic mean	100	71.5	
standard deviation	± 100	± 19.09	-
Sex: Female, Male Units: participants			
Female	0	0	5
Male	1	2	10
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	1	2	14
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	1	1	14
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Phase 1: INCB001158 75 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 75 milligrams (mg) twice daily (BID) in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 1: INCB001158 100 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 2: INCB001158 100 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 2: daratumumab; cross over to INCB001158 + daratumumab

Reporting group description:

In Part 1 of Phase 2, participants received daratumumb 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2 (28-day cycles), once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. At the time of confirmed disease progression, participants crossed over to Part 2 of Phase 2 to receive oral INCB001158 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Reporting group title	Phase 2: INCB001158; cross over to INCB001158 + daratumumab

Reporting group description:

In Part 1 of Phase 2, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1. At the time of confirmed disease progression, participants crossed over to Part 2 of Part 2 to receive oral INCB001158 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Primary: Phase 1: Number of participants with any treatment-emergent adverse event (TEAE)

End point title	Phase 1: Number of participants with any treatment-emergent adverse event (TEAE)[1][2]

End point description:

A TEAE was defined as an adverse event (AE) that was reported for the first time or the worsening of a pre-existing event after the first dose of study treatment.

End point type	Primary

End point timeframe:

up to 454 days

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: Statistical analysis was not conducted for this endpoint.

[2] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	4		
Units: participants	6	4		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Overall Response Rate (ORR): number of participants with a documented response of complete response (CR), stringent CR (sCR), very good partial response (VGPR), or PR, as per International Myeloma Working Group (IMWG) criteria

End point title	Phase 2: Overall Response Rate (ORR): number of participants with a documented response of complete response (CR), stringent CR (sCR), very good partial response (VGPR), or PR, as per International Myeloma Working Group (IMWG) criteria[3][4]

End point description:

CR: negative immunofixation on serum/urine, disappearance of soft tissue plasmacytomas, <5% bone marrow plasma cells (PCs). sCR: defined CR, plus (a) normal free light chain (FLC) ratio, (b) no clonal PCs by immunohistochemistry, immunofluorescence, or 2- to 4-color flow cytometry. VGPR: serum/urine M-component detectable by immunofixation but not on electrophoresis, or ≥90% reduction in serum M-protein (SMP) plus urine M-protein (UMP) <100 milligrams (mg)/24 hours. PR: ≥50% reduction of SMP and reduction in 24-hour UMP by ≥90% or to <200 mg/24 hours. SMP and UMP not measurable: decrease of ≥50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. SMP and UMP not measurable, and serum free light assay is not measurable: ≥50% reduction in bone marrow PCs is required in place of M-protein, if Baseline bone marrow PC percentage was ≥30%. If present at Baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is required.

End point type	Primary

End point timeframe:

up to Day 386

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: Statistical analysis was not conducted for this endpoint.

[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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	1	2	
Units: participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: ORR: number of participants with a documented response of CR, sCR, VGPR, or PR, as per IMWG criteria

End point title	Phase 1: ORR: number of participants with a documented response of CR, sCR, VGPR, or PR, as per IMWG criteria[5]

End point description:

CR: negative immunofixation on serum/urine, disappearance of soft tissue plasmacytomas, <5% bone marrow plasma cells (PCs). sCR: defined CR, plus (a) normal free light chain (FLC) ratio, (b) no clonal PCs by immunohistochemistry, immunofluorescence, or 2- to 4-color flow cytometry. VGPR: serum/urine M-component detectable by immunofixation but not on electrophoresis, or ≥90% reduction in serum M-protein (SMP) plus urine M-protein (UMP) <100 milligrams (mg)/24 hours. PR: ≥50% reduction of SMP and reduction in 24-hour UMP by ≥90% or to <200 mg/24 hours. SMP and UMP not measurable: decrease of ≥50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. SMP and UMP not measurable, and serum free light assay is not measurable: ≥50% reduction in bone marrow PCs is required in place of M-protein, if Baseline bone marrow PC percentage was ≥30%. If present at Baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is required.

End point type	Secondary

End point timeframe:

up to Day 395

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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	4		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of participants with any TEAE

End point title	Phase 2: Number of participants with any TEAE[6]

End point description:

A TEAE was defined as an AE that was reported for the first time or the worsening of a pre-existing event after the first dose of study treatment.

End point type	Secondary

End point timeframe:

up to 420 days

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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	1	2	
Units: participants	1	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to response, defined as the time from the first dose of study drug to the first documented response of PR or better (CR, sCR, VGPR, or PR), as per IMWG criteria

End point title	Phase 1: Time to response, defined as the time from the first dose of study drug to the first documented response of PR or better (CR, sCR, VGPR, or PR), as per IMWG criteria[7]

End point description:

CR: negative immunofixation on serum/urine, disappearance of soft tissue plasmacytomas, <5% bone marrow plasma cells (PCs). sCR: defined CR, plus (a) normal free light chain (FLC) ratio, (b) no clonal PCs by immunohistochemistry, immunofluorescence, or 2- to 4-color flow cytometry. VGPR: serum/urine M-component detectable by immunofixation but not on electrophoresis, or ≥90% reduction in serum M-protein (SMP) plus urine M-protein (UMP) <100 milligrams (mg)/24 hours. PR: ≥50% reduction of SMP and reduction in 24-hour UMP by ≥90% or to <200 mg/24 hours. SMP and UMP not measurable: decrease of ≥50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. SMP and UMP not measurable, and serum free light assay is not measurable: ≥50% reduction in bone marrow PCs is required in place of M-protein, if Baseline bone marrow PC percentage was ≥30%. If present at Baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is required.

End point type	Secondary

End point timeframe:

up to Day 395

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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: days				
median (confidence interval 95%)	(to)	(to)		

Notes:

[8] - No participants had a response of PR or better; thus, analysis was not conducted.

[9] - No participants had a response of PR or better; thus, analysis was not conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to response, defined as the time from the first dose of study drug to the first documented response of PR or better (CR, sCR, VGPR, or PR), as per IMWG criteria

End point title	Phase 2: Time to response, defined as the time from the first dose of study drug to the first documented response of PR or better (CR, sCR, VGPR, or PR), as per IMWG criteria[10]

End point description:

CR: negative immunofixation on serum/urine, disappearance of soft tissue plasmacytomas, <5% bone marrow plasma cells (PCs). sCR: defined CR, plus (a) normal free light chain (FLC) ratio, (b) no clonal PCs by immunohistochemistry, immunofluorescence, or 2- to 4-color flow cytometry. VGPR: serum/urine M-component detectable by immunofixation but not on electrophoresis, or ≥90% reduction in serum M-protein (SMP) plus urine M-protein (UMP) <100 milligrams (mg)/24 hours. PR: ≥50% reduction of SMP and reduction in 24-hour UMP by ≥90% or to <200 mg/24 hours. SMP and UMP not measurable: decrease of ≥50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. SMP and UMP not measurable, and serum free light assay is not measurable: ≥50% reduction in bone marrow PCs is required in place of M-protein, if Baseline bone marrow PC percentage was ≥30%. If present at Baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is required.

End point type	Secondary

End point timeframe:

up to Day 386

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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[11]	0[12]	0[13]	
Units: days				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[11] - No participants had a response of PR or better; thus, analysis was not conducted.

[12] - No participants had a response of PR or better; thus, analysis was not conducted

[13] - No participants had a response of PR or better; thus, analysis was not conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of response, defined as time from first documented response of PR or better (CR, sCR, VGPR, PR), as per IMWG criteria, until date of

disease progression or death, whichever occurred first

End point title	Phase 2: Duration of response, defined as time from first documented response of PR or better (CR, sCR, VGPR, PR), as per IMWG criteria, until date of disease progression or death, whichever occurred first[14]

End point description:

CR: negative immunofixation on serum/urine, disappearance of soft tissue plasmacytomas, <5% bone marrow plasma cells (PCs). sCR: defined CR, plus (a) normal free light chain (FLC) ratio, (b) no clonal PCs by immunohistochemistry, immunofluorescence, or 2- to 4-color flow cytometry. VGPR: serum/urine M-component detectable by immunofixation but not on electrophoresis, or ≥90% reduction in serum M-protein (SMP) plus urine M-protein (UMP) <100 milligrams (mg)/24 hours. PR: ≥50% reduction of SMP and reduction in 24-hour UMP by ≥90% or to <200 mg/24 hours. SMP and UMP not measurable: decrease of ≥50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. SMP and UMP not measurable, and serum free light assay is not measurable: ≥50% reduction in bone marrow PCs is required in place of M-protein, if Baseline bone marrow PC percentage was ≥30%. If present at Baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is required.

End point type	Secondary

End point timeframe:

up to Day 386

Notes:

[14] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: days				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[15] - No participants had a response of PR or better; thus, analysis was not conducted.

[16] - No participants had a response of PR or better; thus, analysis was not conducted.

[17] - No participants had a response of PR or better; thus, analysis was not conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Duration of response, defined as time from first documented response of PR or better (CR, sCR, VGPR, PR), as per IMWG criteria, until date of disease progression or death, whichever occurred first

End point title	Phase 1: Duration of response, defined as time from first documented response of PR or better (CR, sCR, VGPR, PR), as per IMWG criteria, until date of disease progression or death, whichever occurred first[18]

End point description:

CR: negative immunofixation on serum/urine, disappearance of soft tissue plasmacytomas, <5% bone marrow plasma cells (PCs). sCR: defined CR, plus (a) normal free light chain (FLC) ratio, (b) no clonal PCs by immunohistochemistry, immunofluorescence, or 2- to 4-color flow cytometry. VGPR: serum/urine M-component detectable by immunofixation but not on electrophoresis, or ≥90% reduction in serum M-protein (SMP) plus urine M-protein (UMP) <100 milligrams (mg)/24 hours. PR: ≥50% reduction of SMP and reduction in 24-hour UMP by ≥90% or to <200 mg/24 hours. SMP and UMP not measurable: decrease of ≥50% in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria. SMP and UMP not measurable, and serum free light assay is not measurable:

≥50% reduction in bone marrow PCs is required in place of M-protein, if Baseline bone marrow PC percentage was ≥30%. If present at Baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is required.

End point type	Secondary

End point timeframe:

up to Day 395

Notes:

[18] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	0[20]		
Units: days				
median (confidence interval 95%)	(to)	(to)		

Notes:

[19] - No participants had a response of PR or better; thus, analysis was not conducted

[20] - No participants had a response of PR or better; thus, analysis was not conducted

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS), defined as the duration from the date of the first dose of study drug until either progressive disease, as per IMWG criteria, or death, whichever occurred first

End point title	Progression-free survival (PFS), defined as the duration from the date of the first dose of study drug until either progressive disease, as per IMWG criteria, or death, whichever occurred first

End point description:

Progressive disease: increase of 25% from the lowest response value in any one of the following: (a) serum M-component (absolute increase must be ≥0.5 grams per deciliter [g/dL]); (b) urine M-component (absolute increase must be ≥200 mg/24 hours); (c) only in participants without measurable serum and urine M-protein levels: the difference between involved and uninvolved FLC levels (absolute increase must be > 10 mg/dL); (d) only in participants without measurable serum and urine M-protein levels and without measurable disease by FLC levels, bone marrow plasma cell (PC) percentage (absolute percentage must be ≥10%); (d) bone marrow PC percentage: the absolute percentage must be > 10%; (e) definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas; (f) development of hypercalcemia (corrected serum calcium > 11.5 mg/dL) that can be attributed solely to the PC proliferative disorder.

End point type	Secondary

End point timeframe:

up to approximately 2 years

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[21]	4[22]	2[23]	1[24]
Units: days				
Minimum value, uncensored	8	26	9999	9999
Maximum value, uncensored	337	169	9999	9999

Notes:

[21] - PFS was calculated for individual participants; no formal analysis due to a small sample size.

[22] - PFS was calculated for individual participants; no formal analysis due to a small sample size.

[23] - Data cannot be reported; the small sample size could lead to the re-identification of participants.

[24] - Data cannot be reported; the small sample size could lead to the re-identification of participants.

End point values	Phase 2: INCB001158; cross over to INCB001158 + daratumumab			
Subject group type	Reporting group			
Number of subjects analysed	2[25]			
Units: days				
Minimum value, uncensored	9999			
Maximum value, uncensored	9999			

Notes:

[25] - Data cannot be reported; the small sample size could lead to the re-identification of participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Minimal residual disease (MRD), defined as the percentage of MRD-negative participants

End point title	Phase 1: Minimal residual disease (MRD), defined as the percentage of MRD-negative participants[26]

End point description:

Bone marrow aspirate was to be collected for MRD analysis. The MRD assay required an analysis to be performed at Baseline and another analysis to be performed at the time of suspected complete response. At the time enrollment was halted, no participants had a complete response; thus, MRD analysis was not performed.

End point type	Secondary

End point timeframe:

up to approximately 2 years

Notes:

[26] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[27]	0[28]		
Units: percentage of participants				

Notes:

[27] - Analysis was not conducted; no participants had a complete response at time of enrollment halt.

[28] - Analysis was not conducted; no participants had a complete response at time of enrollment halt.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: MRD, defined as the percentage of MRD-negative participants

End point title	Phase 2: MRD, defined as the percentage of MRD-negative participants[29]

End point description:

Bone marrow aspirate was to be collected for MRD analysis. The MRD assay required an analysis to be performed at Baseline and another analysis to be performed at the time of suspected complete response. At the time enrollment was halted, no participants had a complete response; thus, MRD analysis was not performed.

End point type	Secondary

End point timeframe:

up to approximately 2 years

Notes:

[29] - 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: Statistical analysis was not conducted for this endpoint.

End point values	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab	Phase 2: INCB001158; cross over to INCB001158 + daratumumab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[30]	0[31]	0[32]	
Units: percentage of participants				

Notes:

[30] - Analysis was not conducted; no participants had a complete response at time of enrollment halt.

[31] - Analysis was not conducted; no participants had a complete response at time of enrollment halt.

[32] - Analysis was not conducted; no participants had a complete response at time of enrollment halt.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival (OS) was defined as the time from the first dose of study drug to death from any cause until study completion. 9999=Minimum and maximum data values cannot be reported; doing so for the small sample size could lead to the re-identification of participants.

End point type	Secondary

End point timeframe:
up to 923 days (approximately 2.5 years)

End point values	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab	Phase 2: INCB001158 100 mg BID + daratumumab	Phase 2: daratumumab; cross over to INCB001158 + daratumumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6[33]	4[34]	2[35]	1[36]
Units: days				
number (not applicable)				
Minimum value, uncensored	113	127	9999	9999
Maximum value, uncensored	766	604	9999	9999

Notes:
[33] - OS was calculated for individual participants; no formal analysis due to a small sample size.
[34] - OS was calculated for individual participants; no formal analysis due to a small sample size.
[35] - Data cannot be reported; the small sample size could lead to the re-identification of participants.
[36] - Data cannot be reported; the small sample size could lead to the re-identification of participants.

End point values	Phase 2: INCB001158; cross over to INCB001158 + daratumumab			
Subject group type	Reporting group			
Number of subjects analysed	2[37]			
Units: days				
number (not applicable)				
Minimum value, uncensored	9999			
Maximum value, uncensored	9999			

Notes:
[37] - Data cannot be reported; the small sample size could lead to the re-identification of participants.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed for up to 454 days; All-cause Mortality was assessed for up to 923 days (approximately 2.5 years).

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs), defined as adverse events that were reported for the first time or the worsening of pre-existing events after the first dose of study treatment, have been reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Phase 1: INCB001158 75 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 75 milligrams (mg) twice daily (BID) in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Phase 1: INCB001158 100 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Reporting group title	Total

Reporting group description:

Total

Reporting group title	Phase 1/2: daratumumab; cross over to INCB001158 + daratumumab

Reporting group description:

In Phase 1, participants received daratumumb 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2 (28-day cycles), once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. At the time of confirmed disease progression, participants crossed over to Phase 2 to receive oral INCB001158 75 or 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Reporting group title	Phase 1/2: INCB001158; cross over to INCB001158 + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 75 or 100 mg BID in 28-day cycles starting at Cycle 1. At the time of confirmed disease progression, participants crossed over to Part 2 to receive oral INCB001158 75 or 100 mg BID starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment in Phase 2 continued for as long as participants were receiving clinical benefit and did not met any criteria for study withdrawal.

Reporting group title	Phase 2: INCB001158 100 mg BID + daratumumab

Reporting group description:

In Phase 1, participants received oral INCB001158 100 mg BID in 28-day cycles starting at Cycle 1, and 1800 mg subcutaneous daratumumab, administered once weekly for Cycles 1 and 2, once every 2 weeks for Cycles 3 to 6, and once every 4 weeks thereafter. Treatment continued until disease progression, unacceptable toxicity, or discontinuation from study treatment for any other reason.

Serious adverse events	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	1 / 4 (25.00%)	5 / 15 (33.33%)
number of deaths (all causes)	5	2	9
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			

subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1/2: daratumumab; cross over to INCB001158 + daratumumab	Phase 1/2: INCB001158; cross over to INCB001158 + daratumumab	Phase 2: INCB001158 100 mg BID + daratumumab
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Phase 1: INCB001158 75 mg BID + daratumumab	Phase 1: INCB001158 100 mg BID + daratumumab	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	4 / 4 (100.00%)	13 / 15 (86.67%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	4 / 15 (26.67%)
occurrences (all)	0	1	4
Discomfort			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	3 / 6 (50.00%)	0 / 4 (0.00%)	4 / 15 (26.67%)
occurrences (all)	3	0	4
Injection site bruising			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	1 / 4 (25.00%)	3 / 15 (20.00%)
occurrences (all)	1	1	3
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	0	1	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Lung infiltration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	2 / 6 (33.33%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	2	0	2
Productive cough			

subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Pulmonary oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Listless			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Humerus fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Rib fracture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Skin laceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1

Cardiovascular insufficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Dysstasia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	2 / 15 (13.33%)
occurrences (all)	0	1	2
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Neuropathy peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	4
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	3 / 15 (20.00%)
occurrences (all)	0	1	3
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Constipation			

subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)	0 / 4 (0.00%)	3 / 15 (20.00%)
occurrences (all)	3	0	3
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	2 / 4 (50.00%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Ingrowing nail			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Muscle spasms			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	2 / 15 (13.33%)
occurrences (all)	1	0	2
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Musculoskeletal chest pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Oral candidiasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Rhinovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	2
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 4 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	2
Oroticaciduria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 4 (25.00%)	1 / 15 (6.67%)
occurrences (all)	0	1	1

Non-serious adverse events	Phase 1/2: daratumumab; cross over to INCB001158	Phase 1/2: INCB001158; cross over to INCB001158	Phase 2: INCB001158 100 mg BID +

	+ daratumumab	+ daratumumab	daratumumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	1 / 2 (50.00%)
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 1 (100.00%)	1 / 2 (50.00%)	1 / 2 (50.00%)
occurrences (all)	1	1	1
Discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Injection site bruising			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

Lung infiltration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Listless			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Skin laceration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiovascular insufficiency			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysstasia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	4
Lymphopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	1 / 2 (50.00%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Bone pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 2 (50.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			

subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinovirus infection			
subjects affected / exposed	1 / 1 (100.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oroticaciduria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2019	A summary of experimental studies was added to provide evidence to support the biologic rationale for the combination. Updated to allow for 2 cycles of INCB001158 monotherapy instead of 3 cycles in Treatment Group C – Part 1, and to require all participants to have had at least 3 prior treatments. Stopping rules were added for safety in Phase 2. A revision was made to clarify the definition of injection-related reactions (IRRs) and the management of IRRs.
12 October 2020	The primary purpose of this amendment was to introduce a crossover to INCB001158+daratumumab after daratumumab monotherapy.
01 December 2021	The primary purpose of this amendment was to provide guidance for the management of ongoing participants, as enrollment had been terminated and sufficient data had been collected for safety analysis.

Notes:

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.

The study was terminated following a recruitment challenge. There were no safety-related concerns.

Notes: