Clinical trial results:
A randomized, open-label, phase II open platform study evaluating the efficacy and safety of novel spartalizumab (PDR001) combinations in previously treated unresectable or metastatic melanoma

Summary

EudraCT number	2018-000610-38
Trial protocol	GB FR DE NL ES IT
Global end of trial date	30 December 2022

Results information

Result version number	v1 (current)
This version publication date	05 January 2024
First version publication date	05 January 2024

Trial information

Trial identification

Sponsor protocol code	CPDR001J2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03484923
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111, novartis.email@novartis.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 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of each combination arm, as measured by confirmed objective response rate

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	France: 52
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Switzerland: 16
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	196
EEA total number of subjects	133

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)	122
From 65 to 84 years	74
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

None of the arms were opened in the extension part.

Pre-assignment

Screening details:

The screening period began once written informed consent was provided and ended after 28 days (or after 35 days for subjects screened for Arm 1A) or when subject was randomized/enrolled, whichever came first. 1 participant randomized to Arm 3 discontinued before study treatment due to an AE.

Period 1

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

Blinding implementation details:

After approval of protocol amendment 5 (26Jun2020), a non-randomized single arm was added

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1: LAG525 + PDR001 (randomized section)

Arm description:

Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Ieramilimab
Investigational medicinal product code	LAG525
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg of LAG525 administered every 4 weeks intravenously

Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg of PDR001 administered every 4 weeks intravenously

Arm title	Arm 2: INC280+PDR001 (randomized section)

Arm description:

Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Capmatinib
Investigational medicinal product code	INC280
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg of INC280 administered twice daily orally

Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg of PDR001 administered every 4 weeks intravenously

Arm title	Arm 3: ACZ885 + PDR001 (randomized section)

Arm description:

Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Canakinumab
Investigational medicinal product code	ACZ885
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg of ACZ885 administered every 4 weeks subcutaneosuly

Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg of PDR001 administered every 4 weeks intravenously

Arm title	Arm 4: LEE011 + PDR001 (randomized section)

Arm description:

Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Ribociclib
Investigational medicinal product code	LEE011
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

600 mg of LEE011 orally taken once daily on Days 1-21 of a 28-day cycle

Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg of PDR001 administered every 4 weeks intravenously

Arm title	Arm 1A: LAG525 + PDR001 (non-randomized section)

Arm description:

LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks

Arm type	Experimental

Investigational medicinal product name	Ieramilimab
Investigational medicinal product code	LAG525
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

600 mg of LAG525 administered every 4 weeks intravenously

Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg of PDR001 administered every 4 weeks intravenously

Number of subjects in period 1	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)
Started	45	43	43
Treated	45	43	42
Completed	0	0	0
Not completed	45	43	43
Physician decision	6	7	6
Subject Decision	1	3	3
Adverse event, non-fatal	3	3	5
Death	2	2	3
Progressive disease	33	28	26

Number of subjects in period 1	Arm 4: LEE011 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)
Started	44	21
Treated	44	21
Completed	0	0
Not completed	44	21
Physician decision	3	2
Subject Decision	-	1
Adverse event, non-fatal	11	1
Death	-	1
Progressive disease	30	16

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1: LAG525 + PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 2: INC280+PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 3: ACZ885 + PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 4: LEE011 + PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 1A: LAG525 + PDR001 (non-randomized section)
Reporting group description:	
LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	

Reporting group values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)
Number of subjects	45	43	43
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	29	29	28
>=65 years	16	14	15
Sex: Female, Male Units: Participants			
Female	17	21	15
Male	28	22	28
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	45	42	38
More than one race	0	0	0
Unknown or Not Reported	0	1	4

Reporting group values	Arm 4: LEE011 + PDR001 (randomized	Arm 1A: LAG525 + PDR001 (non-randomized section)	Total

section)

Number of subjects	44	21	196
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	28	8	122
>=65 years	16	13	74
Sex: Female, Male Units: Participants			
Female	14	9	76
Male	30	12	120
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	42	20	187
More than one race	0	0	0
Unknown or Not Reported	2	0	7

End points

End points reporting groups

Reporting group title	Arm 1: LAG525 + PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 2: INC280+PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 3: ACZ885 + PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 4: LEE011 + PDR001 (randomized section)
Reporting group description:	
Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Reporting group title	Arm 1A: LAG525 + PDR001 (non-randomized section)
Reporting group description:	
LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1]
End point description:	
ORR defined as the percentage of patients with a best overall response of either confirmed complete response (CR) or partial response (PR) as per local review by Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) and assessed by computed tomography (CT)/ magnetic resonance imaging (MRI). CR:Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.	
End point type	Primary
End point timeframe:	
Up to 49 months (randomized section) and 18 months (non-randomized section)	

Notes:

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

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	43	43	44
Units: Percentage of participants				
number (confidence interval 95%)	8.9 (2.5 to 21.2)	4.7 (0.6 to 15.8)	4.7 (0.6 to 15.8)	6.8 (1.4 to 18.7)

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Percentage of participants				
number (confidence interval 95%)	14.3 (3.0 to 36.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR defined as the time from date of first documented CR or PR to date of first documented disease progression (as per local review by RECIST v1.1 and assessed by CT/MRI) or death due to any cause. Subjects continuing without progression or death due to underlying cancer were censored at the date of their last adequate tumor assessment.
CR:Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

From first documented response to disease progression or death due to any cause, whichever occurs first, assessed up to 49 months (randomized part) and 18 months (non-randomized part)

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	2	2	3
Units: Days				
median (full range (min-max))	476 (169 to 1373)	941.5 (504 to 1379)	617.5 (113 to 1122)	217 (169 to 281)

End point values	Arm 1A: LAG525 + PDR001 (non-randomized			

	section)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Days				
median (full range (min-max))	281 (169 to 449)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from date of randomization (or date of first dose of study treatment in non-randomized part) to date of death due to any cause. The OS distribution was estimated using the Kaplan-Meier method, and the medians and 95% confidence intervals of the medians were presented.

End point type	Secondary

End point timeframe:

From randomization (or start of treatment for non-randomized section) to death due to any cause, assessed up to 49 months (randomized section) and 24 months (non-randomized section)

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	43	43	44
Units: Months				
median (confidence interval 95%)	8.8 (6.3 to 21.4)	12.1 (6.6 to 18.5)	8.7 (5.7 to 17.9)	10.1 (7.4 to 15.6)

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Months				
median (confidence interval 95%)	14.0 (8.4 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR was defined as the percentage of participants with best overall response of CR, PR or stable disease (SD) (as per local review by RECIST v1.1 and assessed by CT/MRI).
CR:Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm
PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary

End point timeframe:

Up to 49 months (randomized section) and 18 months (non-randomized section)

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	43	43	44
Units: Percentage of participants				
number (confidence interval 95%)	15.6 (6.5 to 29.5)	16.3 (6.8 to 30.7)	18.6 (8.4 to 33.4)	31.8 (18.6 to 47.6)

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Percentage of participants				
number (confidence interval 95%)	33.3 (14.6 to 57.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the time between the date of randomization (or date of first dose of study treatment

in non-randomized section) to the date of event defined as the first documented disease progression (as per local review by RECIST v1.1 and assessed by CT/MRI) or death due to any cause. If a subject had not had an event before leaving study or initiation of subsequent anticancer therapy, PFS was censored at the date of last adequate tumor assessment. The PFS distribution was estimated using the Kaplan-Meier method, medians and 95% confidence interval of the medians were presented.

End point type	Secondary

End point timeframe:

From randomization (or start of treatment for non-randomized section) to disease progression or death due to any cause, whichever occurs first, assessed up to 49 months (randomized section) and 18 months (non-randomized section)

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	43	43	44
Units: Months				
median (confidence interval 95%)	2.7 (1.7 to 2.8)	2.7 (2.4 to 2.8)	2.7 (2.6 to 2.8)	2.8 (2.7 to 4.4)

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Months				
median (confidence interval 95%)	2.8 (2.7 to 4.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with PDR001 Anti-drug antibodies (ADA) positive result at baseline

End point title	Percentage of participants with PDR001 Anti-drug antibodies (ADA) positive result at baseline

End point description:

Percentage of participants who had a PDR001 ADA positive result at baseline.

End point type	Secondary

End point timeframe:

At Baseline

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	38	40	41
Units: Participants	1	0	1	0

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for PDR001

End point title	Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for PDR001

End point description:

Percentage of participants who tested positive for treatment-induced ADA for PDR001 (subjects with ADA-negative sample at baseline with at least one post-baseline ADA positive sample) as well as treatment-boosted ADA for PDR001 (subjects with baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment).

End point type	Secondary

End point timeframe:

Pre-infusion on Day 1 of Cycle 1, 2, 3, 4, 5, 6 and thereafter every 3 cycles until end of treatment (EOT), EOT, and 30 and 150 days post-EOT (assessed up to 49 months randomized section and 24 months non-randomized section). Cycle= 28 days

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	34	38	39
Units: Participants	3	5	3	0

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ACZ885 Anti-drug antibodies (ADA) positive result at baseline

End point title	Percentage of participants with ACZ885 Anti-drug antibodies (ADA) positive result at baseline[2]

End point description:

Percentage of participants who had an ACZ885 ADA positive result at baseline. Only applicable for subjects enrolled in Arm 3.

End point type	Secondary

End point timeframe:

At Baseline

Notes:

[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: This endpoint is reporting results for the participants who received ACZ885 (Arm 3)

End point values	Arm 3: ACZ885 + PDR001 (randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with LAG525 Anti-drug antibodies (ADA) positive result at baseline

End point title	Percentage of participants with LAG525 Anti-drug antibodies (ADA) positive result at baseline[3]

End point description:

Percentage of participants who had a LAG525 ADA positive result at baseline. Only applicable for participants enrolled in Arm 1 and Arm 1A.

End point type	Secondary

End point timeframe:

At Baseline

Notes:

[3] - 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: This endpoint is reporting results for the participants who received LAG525 (Arm 1 and Arm 1a)

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	20		
Units: Participants	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for LAG525

End point title	Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for LAG525[4]

End point description:

Percentage of participants who tested positive for treatment-induced ADA for LAG525 (subjects with ADA-negative sample at baseline with at least one post-baseline ADA positive sample) as well as treatment-boosted ADA for LAG525 (subjects with baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment). Only applicable for subjects enrolled in Arm 1 and Arm 1A.

End point type	Secondary

End point timeframe:

Pre-infusion on Day 1 of Cycle 1, 2, 3, 4, 5, 6 and thereafter every 3 cycles until end of treatment (EOT) and EOT (assessed up to 49 months in the randomized section and 18 months in the non-randomized section). Cycle= 28 days

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: This endpoint is reporting results for the participants who received LAG525 (Arm 1 and Arm 1a)

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	19		
Units: Participants	7	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for ACZ885

End point title	Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for ACZ885[5]

End point description:

Percentage of participants who tested positive for treatment-induced ADA for ACZ885 (subjects with ADA-negative sample at baseline with at least one post-baseline ADA positive sample) as well as treatment-boosted ADA for ACZ885 (subjects with baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment). Only applicable for subjects enrolled in Arm 3.

End point type	Secondary

End point timeframe:

Pre-infusion on Day 1 of Cycle 1, 2, 3, 4, 5, 6 and thereafter every 3 cycles until end of treatment (EOT) and EOT (assessed up to 40 months). Cycle= 28 days

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: This endpoint is reporting results for the participants who received ACZ885 (Arm 3)

End point values	Arm 3: ACZ885 + PDR001 (randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a favorable biomarker profile (pFBP)

End point title	Percentage of participants with a favorable biomarker profile (pFBP)

End point description:

Biomarker parameters included: 1) number of tumor infiltrating T cells (TIL), 2) activation level of TIL, and 3) changes in immune response gene expression signatures. For the number of TILs, an increase in tumoral CD8+ cell numbers compared to baseline was considered favorable. The activation level of TIL was assessed by the percentage of tumoral CD8+ cells expressing GzmB (a marker for cytotoxic activity) or Ki67 (a marker for cell proliferation), where an increase in either GZMB+/CD8+ or KI67+/CD8+ post-baseline was considered favorable. Changes in immune response gene expression signatures were evaluated by the levels in T-cell inflamed signature (TIS), where an increase from baseline was considered favorable.
To be categorized as having a pFBP, a subject must meet the favorable criteria for at least two of the three biomarker parameters. The percentage of participants with pFBP was assessed.

End point type	Secondary

End point timeframe:

Baseline and after 3-4 weeks of treatment

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	21	31	6
Units: Percentage of participants				
number (confidence interval 95%)	13.6 (2.9 to 34.9)	4.8 (0.1 to 23.8)	6.5 (0.8 to 21.4)	16.7 (0.4 to 64.1)

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[6] - No patients were analyzed for this arm group

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

Pre-treatment: deaths collected from day of patient’s informed consent to the day before the first administration of study treatment.
On-treatment: deaths collected from start of treatment to 30 days after last dose of study treatment.
Extended safety follow-up: deaths collected from 31 days after last dose of study treatment up to 150 days after last dose of PDR001 (if this timepoint was later than 30 days after last dose of study treatment)
Post-treatment survival follow-up: deaths collected from day 151 post-last dose of PDR001 or 31 days after last dose of study treatment (whichever occurred last) up to end of study.

End point type	Post-hoc

End point timeframe:

Pre-treatment: up to 28/35 days (randomized/non-randomized). On-treatment: up to 49/19 months (randomized/non-randomized). Extended safety FU and Post-treatment survival FU: up to 49/24 months (randomized/non-randomized).

End point values	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	43	43	44
Units: Participants				

Pre-treatment deaths	0	0	0	0
On-treatment deaths	5	3	3	3
Extended safety follow-up deaths	14	11	15	11
Post-treatment survival follow-up deaths	18	19	15	19
All deaths	37	33	33	33

End point values	Arm 1A: LAG525 + PDR001 (non-randomized section)			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Participants				
Pre-treatment deaths	0			
On-treatment deaths	1			
Extended safety follow-up deaths	4			
Post-treatment survival follow-up deaths	7			
All deaths	12			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose up to 150 days after last dose of PDR001 or up to 30 days after last dose of study treatment, (whichever occurred last).assessed up to 49 months (randomized) or 24 months (non-randomized)

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Arm 1: LAG525+PDR001 (randomized part)- extended safety FU

Reporting group description:

AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])

Reporting group title	Arm 1: LAG525+PDR001 (randomized part)- on-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Arm 2: INC280+PDR001 (randomized part)- on-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Arm 2: INC280+PDR001 (randomized part) - extended safety FU

Reporting group description:

AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])

Reporting group title	Arm 3: ACZ885+PDR001 (randomized part)- on-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Arm 3: ACZ885+PDR001 (randomized part)- extended safety FU

Reporting group description:

AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])

Reporting group title	Arm 4: LEE011+PDR001 (randomized part)- on-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Arm 4: LEE011+PDR001 (randomized part)- extended safety FU

Reporting group description:

AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])

Reporting group title	Arm 1A: LAG525+PDR001 (non-randomized part)- on-treatment

Reporting group description:

AEs collected during on-treatment period (up to 30 days post-treatment)

Reporting group title	Arm 1A: LAG525+PDR001 (non-randomized part)-extended safety FU

Reporting group description:

AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])

Serious adverse events	Arm 1: LAG525+PDR001 (randomized part)-extended safety FU	Arm 1: LAG525+PDR001 (randomized part)-on-treatment	Arm 2: INC280+PDR001 (randomized part)-on-treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 45 (11.11%)	21 / 45 (46.67%)	21 / 43 (48.84%)
number of deaths (all causes)	14	5	3
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 43 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast neoplasm			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Metastases to bone			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Metastases to spleen			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oncologic complication			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 45 (2.22%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Peripheral ischaemia			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Vena cava thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Chest pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Heteroplasia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 43 (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
Pyrexia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Haemothorax			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Pleural effusion			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Investigations			
Blood lactic acid increased			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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 physical condition abnormal			
subjects affected / exposed	1 / 45 (2.22%)	2 / 45 (4.44%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Liver function test increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Humerus fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular procedural complication			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Diabetic hyperglycaemic coma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglossal nerve disorder			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Seizure			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral nerve paresis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Nervous system disorder			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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			
Abdominal pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	2 / 43 (4.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Diarrhoea			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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 haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Intussusception			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Nausea			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Subileus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Vomiting			

subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cytolysis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Hypertransaminasaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Adrenal haematoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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 in extremity			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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			
Infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Pneumonia			
subjects affected / exposed	2 / 45 (4.44%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 45 (0.00%)	0 / 43 (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
Sepsis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Skin infection			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspected COVID-19			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Cachexia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Diabetes mellitus			

subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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
Hyponatraemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (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

Serious adverse events	Arm 2: INC280+PDR001 (randomized part) - extended safety FU	Arm 3: ACZ885+PDR001 (randomized part)- on-treatment	Arm 3: ACZ885+PDR001 (randomized part)- extended safety FU
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	12 / 42 (28.57%)	4 / 42 (9.52%)
number of deaths (all causes)	11	3	15
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Breast neoplasm			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Metastases to bone			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Metastases to spleen			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Oncologic complication			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Tumour pain			

subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hypotension			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena cava thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Phlebitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Venous thrombosis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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			
Asthenia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Chest pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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 physical health deterioration			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Heteroplasia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Oedema peripheral			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Immune system disorders			

Cytokine release syndrome			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Drug hypersensitivity			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Pleural effusion			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Pulmonary embolism			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood lactic acid increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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 physical condition abnormal			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Liver function test abnormal			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Liver function test increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Injury, poisoning and procedural			

complications			
Femur fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Humerus fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Ocular procedural complication			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Myocarditis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Nervous system disorders			
Diabetic hyperglycaemic coma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Cerebral haemorrhage			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Dizziness			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Epilepsy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hypoglossal nerve disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Headache			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hemiparesis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Spinal cord compression			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Seizure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral nerve paresis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Nervous system disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Anaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Dysphagia			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Diarrhoea			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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 haemorrhage			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Intestinal obstruction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Lower gastrointestinal haemorrhage			

subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Subileus			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Vomiting			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hepatic cytolysis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hepatitis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hepatitis acute			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hypertransaminasaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Immune-mediated hepatitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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

Adrenal haematoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Back pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Myositis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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 in extremity			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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			
Infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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

Erysipelas			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Cellulitis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Sepsis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Skin infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Suspected COVID-19			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Dehydration			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Diabetes mellitus			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hypokalaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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
Hyponatraemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (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

Serious adverse events	Arm 4: LEE011+PDR001 (randomized part)- on-treatment	Arm 4: LEE011+PDR001 (randomized part)- extended safety FU	Arm 1A: LAG525+PDR001 (non-randomized part)- on-treatment
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 44 (50.00%)	8 / 44 (18.18%)	7 / 21 (33.33%)
number of deaths (all causes)	3	11	1

number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Breast neoplasm			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Metastases to central nervous system			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Metastases to spleen			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Oncologic complication			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Tumour pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Hypotension			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Vena cava thrombosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Phlebitis			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Venous thrombosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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			
Asthenia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 44 (2.27%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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 physical health deterioration			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Heteroplasia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Oedema peripheral			

subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Pyrexia			
subjects affected / exposed	2 / 44 (4.55%)	2 / 44 (4.55%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Drug hypersensitivity			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Dyspnoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Haemothorax			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Pulmonary embolism			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Investigations			
Blood lactic acid increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
General physical condition abnormal			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Haemoglobin decreased			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Liver function test abnormal			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Humerus fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Ocular procedural complication			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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

Myocarditis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Nervous system disorders			
Diabetic hyperglycaemic coma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Cerebral haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Dizziness			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Facial paresis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Epilepsy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Hypoglossal nerve disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Headache			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Hemiparesis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Spinal cord compression			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Peripheral nerve paresis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Nervous system disorder			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Anaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Autoimmune colitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Dysphagia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Intussusception			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Nausea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Drug-induced liver injury			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Hepatic cytolysis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Hypertransaminasaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Acute kidney injury			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Adrenal haematoma			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Back pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Myositis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	2 / 44 (4.55%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rhabdomyolysis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Infections and infestations			
Infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Erysipelas			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Cellulitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Pneumonia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Sepsis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Skin infection			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Suspected COVID-19			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Cachexia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Dehydration			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Diabetes mellitus			
subjects affected / exposed	0 / 44 (0.00%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoalbuminaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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
Hypokalaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (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
Hyponatraemia			

subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (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

Serious adverse events	Arm 1A: LAG525+PDR001 (non-randomized part)-extended safety FU		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast neoplasm			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to bone			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to spleen				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oncologic complication				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transitional cell carcinoma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep vein thrombosis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vena cava thrombosis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phlebitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Heteroplasia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Cytokine release syndrome				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug hypersensitivity				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Pelvic pain				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemothorax			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood lactic acid increased			

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical condition abnormal				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoglobin decreased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ocular procedural complication				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				

Atrial fibrillation				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Diabetic hyperglycaemic coma				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial paresis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglossal nerve disorder				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral nerve paresis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorder				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Autoimmune colitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated enterocolitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intussusception				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic cytolysis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertransaminasaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated hepatitis			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adrenal haematoma			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myositis			

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				

subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suspected COVID-19				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cachexia				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm 1: LAG525+PDR001 (randomized part)-extended safety FU	Arm 1: LAG525+PDR001 (randomized part)-on-treatment	Arm 2: INC280+PDR001 (randomized part)-on-treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 45 (11.11%)	40 / 45 (88.89%)	42 / 43 (97.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
Tumour pain			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	1 / 43 (2.33%)
occurrences (all)	0	2	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			

Chills			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	3 / 43 (6.98%)
occurrences (all)	0	1	3
Chest pain			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	3 / 43 (6.98%)
occurrences (all)	0	2	3
Asthenia			
subjects affected / exposed	1 / 45 (2.22%)	9 / 45 (20.00%)	7 / 43 (16.28%)
occurrences (all)	1	18	7
Fatigue			
subjects affected / exposed	1 / 45 (2.22%)	7 / 45 (15.56%)	5 / 43 (11.63%)
occurrences (all)	1	7	6
Oedema peripheral			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	10 / 43 (23.26%)
occurrences (all)	0	3	13
Pain			
subjects affected / exposed	0 / 45 (0.00%)	4 / 45 (8.89%)	0 / 43 (0.00%)
occurrences (all)	0	4	0
Pyrexia			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	13 / 43 (30.23%)
occurrences (all)	0	3	16
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	8 / 43 (18.60%)
occurrences (all)	0	3	9
Dyspnoea			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	6 / 43 (13.95%)
occurrences (all)	0	1	7
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	5 / 43 (11.63%)
occurrences (all)	0	1	6

Amylase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	6 / 43 (13.95%)
occurrences (all)	0	1	7
Blood creatinine increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	5 / 43 (11.63%)
occurrences (all)	0	0	5
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 45 (0.00%)	4 / 45 (8.89%)	2 / 43 (4.65%)
occurrences (all)	0	4	3
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 45 (4.44%)	3 / 45 (6.67%)	0 / 43 (0.00%)
occurrences (all)	1	4	0
Lipase increased			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	3 / 43 (6.98%)
occurrences (all)	1	3	3
Haemoglobin decreased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	2 / 43 (4.65%)
occurrences (all)	0	1	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 45 (2.22%)	2 / 45 (4.44%)	2 / 43 (4.65%)
occurrences (all)	1	2	2
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			

subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	3 / 43 (6.98%)
occurrences (all)	0	3	4
Neutrophil count decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	0 / 45 (0.00%)	6 / 45 (13.33%)	2 / 43 (4.65%)
occurrences (all)	0	7	2
White blood cell count decreased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	5 / 43 (11.63%)
occurrences (all)	0	9	7
Dizziness			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	2 / 43 (4.65%)
occurrences (all)	0	3	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 45 (4.44%)	3 / 45 (6.67%)	6 / 43 (13.95%)
occurrences (all)	2	4	6
Eosinophilia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	1 / 45 (2.22%)	1 / 45 (2.22%)	1 / 43 (2.33%)
occurrences (all)	1	1	1
Lymphopenia			
subjects affected / exposed	1 / 45 (2.22%)	2 / 45 (4.44%)	2 / 43 (4.65%)
occurrences (all)	0	4	2
Leukopenia			

subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	0 / 43 (0.00%)
occurrences (all)	0	2	0
Neutropenia			
subjects affected / exposed	1 / 45 (2.22%)	3 / 45 (6.67%)	0 / 43 (0.00%)
occurrences (all)	0	8	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 45 (0.00%)	6 / 45 (13.33%)	10 / 43 (23.26%)
occurrences (all)	0	7	12
Abdominal pain			
subjects affected / exposed	1 / 45 (2.22%)	5 / 45 (11.11%)	3 / 43 (6.98%)
occurrences (all)	1	8	4
Constipation			
subjects affected / exposed	0 / 45 (0.00%)	8 / 45 (17.78%)	6 / 43 (13.95%)
occurrences (all)	0	8	6
Nausea			
subjects affected / exposed	0 / 45 (0.00%)	13 / 45 (28.89%)	18 / 43 (41.86%)
occurrences (all)	0	18	22
Dry mouth			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
Vomiting			
subjects affected / exposed	0 / 45 (0.00%)	6 / 45 (13.33%)	11 / 43 (25.58%)
occurrences (all)	0	10	14
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 45 (0.00%)	0 / 45 (0.00%)	1 / 43 (2.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 45 (0.00%)	11 / 45 (24.44%)	6 / 43 (13.95%)
occurrences (all)	0	14	6
Rash			

subjects affected / exposed	0 / 45 (0.00%)	4 / 45 (8.89%)	8 / 43 (18.60%)
occurrences (all)	0	5	9
Vitiligo			
subjects affected / exposed	0 / 45 (0.00%)	4 / 45 (8.89%)	0 / 43 (0.00%)
occurrences (all)	0	4	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 45 (0.00%)	2 / 45 (4.44%)	2 / 43 (4.65%)
occurrences (all)	0	2	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 45 (2.22%)	5 / 45 (11.11%)	2 / 43 (4.65%)
occurrences (all)	0	7	2
Pain in extremity			
subjects affected / exposed	0 / 45 (0.00%)	5 / 45 (11.11%)	3 / 43 (6.98%)
occurrences (all)	0	5	3
Back pain			
subjects affected / exposed	0 / 45 (0.00%)	5 / 45 (11.11%)	4 / 43 (9.30%)
occurrences (all)	0	7	4
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 45 (0.00%)	3 / 45 (6.67%)	3 / 43 (6.98%)
occurrences (all)	0	3	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 45 (0.00%)	10 / 45 (22.22%)	3 / 43 (6.98%)
occurrences (all)	0	10	3
Hypoalbuminaemia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 45 (2.22%)	3 / 43 (6.98%)
occurrences (all)	0	1	3

Non-serious adverse events	Arm 2: INC280+PDR001 (randomized part) - extended safety FU	Arm 3: ACZ885+PDR001 (randomized part)- on-treatment	Arm 3: ACZ885+PDR001 (randomized part)- extended safety FU
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 43 (13.95%)	32 / 42 (76.19%)	5 / 42 (11.90%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Tumour pain			
subjects affected / exposed	1 / 43 (2.33%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	1 / 43 (2.33%)	7 / 42 (16.67%)	0 / 42 (0.00%)
occurrences (all)	1	9	0
Fatigue			
subjects affected / exposed	0 / 43 (0.00%)	5 / 42 (11.90%)	1 / 42 (2.38%)
occurrences (all)	0	6	1
Oedema peripheral			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	3	0

Dyspnoea			
subjects affected / exposed	0 / 43 (0.00%)	8 / 42 (19.05%)	0 / 42 (0.00%)
occurrences (all)	0	8	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
Amylase increased			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	5	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	1 / 42 (2.38%)
occurrences (all)	0	2	0
Blood creatinine increased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	6	0
Haemoglobin decreased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test negative			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 43 (0.00%)	5 / 42 (11.90%)	1 / 42 (2.38%)
occurrences (all)	0	5	1
White blood cell count decreased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	5	0
Dizziness			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	6 / 42 (14.29%)	1 / 42 (2.38%)
occurrences (all)	1	7	1
Eosinophilia			

subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
Thrombocytopenia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 43 (2.33%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	1	6	0
Abdominal pain			
subjects affected / exposed	0 / 43 (0.00%)	5 / 42 (11.90%)	0 / 42 (0.00%)
occurrences (all)	0	10	0
Constipation			
subjects affected / exposed	1 / 43 (2.33%)	7 / 42 (16.67%)	0 / 42 (0.00%)
occurrences (all)	1	7	0
Nausea			
subjects affected / exposed	0 / 43 (0.00%)	9 / 42 (21.43%)	1 / 42 (2.38%)
occurrences (all)	0	15	1
Dry mouth			
subjects affected / exposed	0 / 43 (0.00%)	4 / 42 (9.52%)	0 / 42 (0.00%)
occurrences (all)	0	4	0
Vomiting			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	6	0
Hepatobiliary disorders			
Hepatic cytolysis			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
Rash			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	0 / 42 (0.00%)
occurrences (all)	0	3	0
Vitiligo			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			
subjects affected / exposed	2 / 43 (4.65%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Back pain			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Rhinitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 43 (2.33%)	7 / 42 (16.67%)	0 / 42 (0.00%)
occurrences (all)	1	7	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 42 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Arm 4: LEE011+PDR001 (randomized part)- on-treatment	Arm 4: LEE011+PDR001 (randomized part)- extended safety FU	Arm 1A: LAG525+PDR001 (non-randomized part)- on-treatment
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)	9 / 44 (20.45%)	18 / 21 (85.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 44 (2.27%)	1 / 44 (2.27%)	2 / 21 (9.52%)
occurrences (all)	1	1	2
Tumour pain			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	8 / 44 (18.18%)	2 / 44 (4.55%)	7 / 21 (33.33%)
occurrences (all)	12	1	7
Fatigue			
subjects affected / exposed	8 / 44 (18.18%)	1 / 44 (2.27%)	4 / 21 (19.05%)
occurrences (all)	9	1	4
Oedema peripheral			

subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	4	0	1
Pain			
subjects affected / exposed	0 / 44 (0.00%)	2 / 44 (4.55%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	8 / 44 (18.18%)	2 / 44 (4.55%)	2 / 21 (9.52%)
occurrences (all)	14	2	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 44 (18.18%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	8	1	0
Dyspnoea			
subjects affected / exposed	4 / 44 (9.09%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	4	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	4	0	1
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	17 / 44 (38.64%)	1 / 44 (2.27%)	1 / 21 (4.76%)
occurrences (all)	25	0	1
Amylase increased			
subjects affected / exposed	3 / 44 (6.82%)	1 / 44 (2.27%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Alanine aminotransferase increased			
subjects affected / exposed	15 / 44 (34.09%)	2 / 44 (4.55%)	1 / 21 (4.76%)
occurrences (all)	20	1	1
Blood creatinine increased			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Blood lactate dehydrogenase			

increased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Lipase increased			
subjects affected / exposed	5 / 44 (11.36%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	9	0	2
Haemoglobin decreased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 44 (6.82%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	3	1	0
Electrocardiogram QT prolonged			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Blood potassium decreased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	0	0	2
SARS-CoV-2 test negative			
subjects affected / exposed	4 / 44 (9.09%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	5	2	0
Platelet count decreased			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	6	0	0
Neutrophil count decreased			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Weight decreased			
subjects affected / exposed	4 / 44 (9.09%)	2 / 44 (4.55%)	0 / 21 (0.00%)
occurrences (all)	4	2	0
White blood cell count decreased			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Nervous system disorders			

Paraesthesia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	3	0	2
Headache			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	4	0	2
Dizziness			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	3	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 44 (25.00%)	0 / 44 (0.00%)	3 / 21 (14.29%)
occurrences (all)	17	0	4
Eosinophilia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Lymphopenia			
subjects affected / exposed	7 / 44 (15.91%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	8	0	1
Leukopenia			
subjects affected / exposed	4 / 44 (9.09%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	4	0	0
Neutropenia			
subjects affected / exposed	20 / 44 (45.45%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	53	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 44 (20.45%)	1 / 44 (2.27%)	5 / 21 (23.81%)
occurrences (all)	11	1	9
Abdominal pain			
subjects affected / exposed	5 / 44 (11.36%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	6	0	2
Constipation			

subjects affected / exposed	3 / 44 (6.82%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	3	1	0
Nausea			
subjects affected / exposed	15 / 44 (34.09%)	2 / 44 (4.55%)	6 / 21 (28.57%)
occurrences (all)	21	2	6
Dry mouth			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	1 / 21 (4.76%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	8 / 44 (18.18%)	1 / 44 (2.27%)	3 / 21 (14.29%)
occurrences (all)	11	1	3
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	7	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	3 / 44 (6.82%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	3	0	0
Pruritus			
subjects affected / exposed	8 / 44 (18.18%)	1 / 44 (2.27%)	3 / 21 (14.29%)
occurrences (all)	12	1	3
Rash			
subjects affected / exposed	4 / 44 (9.09%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	4	1	0
Vitiligo			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	2	0	2
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	1	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 44 (4.55%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0

Pain in extremity			
subjects affected / exposed	3 / 44 (6.82%)	1 / 44 (2.27%)	0 / 21 (0.00%)
occurrences (all)	3	1	0
Back pain			
subjects affected / exposed	6 / 44 (13.64%)	0 / 44 (0.00%)	2 / 21 (9.52%)
occurrences (all)	7	0	2
Infections and infestations			
Rhinitis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 44 (20.45%)	2 / 44 (4.55%)	2 / 21 (9.52%)
occurrences (all)	10	2	2
Hypoalbuminaemia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 44 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Arm 1A: LAG525+PDR001 (non-randomized part)-extended safety FU		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Tumour pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chills			

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Amylase increased			

subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Alanine aminotransferase increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Blood creatinine increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Lipase increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Haemoglobin decreased				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Blood potassium decreased				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
SARS-CoV-2 test negative				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Platelet count decreased				

subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 21 (4.76%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Leukopenia			

subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		
Hepatobiliary disorders Hepatic cytolysis subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash	 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 		

subjects affected / exposed occurrences (all) Vitiligo subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		
Infections and infestations Rhinitis subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypoalbuminaemia subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2018	Amendment 1 was required to implement specific feedback received from the US FDA, the Medicines and Healthcare products Regulatory Agency, the German Paul -Ehrlich Institute, and the French health authority (Agence Nationale de Sécurité du Medicament) upon review of the protocol, as well as additional changes. Major changes included: Updating and clarifying inclusion and exclusion criteria; Addition of 2 additional criteria for continuation of study treatment beyond disease progression per RECIST v1.1; Provide additional and modify existing dose modification guidelines; Update the study procedure schedule; Implement a Safety DMC during expansion phase of the study
06 February 2019	Amendment 2 was required to implement feedback from the French HA (Agence Nationale de Sécurité du Medicament) after their review of protocol amendment 1. This amendment implemented precautionary on-treatment monitoring measures to optimize the detection of possible autoimmune myocarditis events in Arm 1 combining PDR001 and LAG525. Guidelines for the management of myocarditis events (of any grade) were revised.
29 April 2019	Amendment 3 was required in order to add a new combination arm for evaluation in this study (Arm 4: LEE011 in combination with PDR001).
24 January 2020	The main purpose of amendment 4 was to amend LEE011's dose modification guidelines for ILD/pneumonitis and TEN, following the observation of rare cases of ILD/pneumonitis in subjects receiving CDK4/6 inhibitors, and the reporting of TEN in the post-marketing setting in a well-documented literature case report (no case observed in the clinical trials).
26 June 2020	The main purpose of amendment 5 was to add a new non-randomized single-arm (Arm 1A) in this study to evaluate the efficacy and safety of PDR001 and LAG525 combination in LAG-3 positive subjects with previously treated unresectable or metastatic melanoma.

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.

Due to EudraCT system limitations, which EMA is aware of, data using 9999 as data points in this record are not an accurate representation of the clinical trial results.
Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results.

Notes: