Clinical trial results:
A phase II open-label, randomized, three-arm, multicenter study of LAG525 given in combination with spartalizumab (PDR001), or with spartalizumab and carboplatin, or with carboplatin, as first or second line therapy in patients with advanced triple-negative breast cancer

Summary

EudraCT number	2017-004865-28
Trial protocol	GB BE FR DE HU ES IT
Global end of trial date	24 November 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	CLAG525B2101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03499899
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 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	24 November 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to assess the antitumor activity of the three treatment arms LAG525 + spartalizumab, LAG525 + spartalizumab + carboplatin and LAG525 + carboplatin, in patients with advanced triple-negative breast cancer (TNBC) in first or second line of therapy, as measured by the overall response rate (ORR) per investigator's assessment according to RECIST v1.1.

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	09 March 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Lebanon: 6
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	Thailand: 1
Country: Number of subjects enrolled	United States: 4

Worldwide total number of subjects	88
EEA total number of subjects	33

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)	76
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted across 33 centers in 17 countries.

Pre-assignment

Screening details:

A total of 132 participants were screened of which 88 participants were enrolled in the study and 87 participants received at least one dose of study treatment (1 participant was not treated due to physician decision)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LAG525 + PDR001

Arm description:

Participants received LAG525 and PDR001 administered as infusion once every 3 weeks

Arm type	Experimental
Investigational medicinal product name	Spartalizumab
Investigational medicinal product code	PDR001
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Spartalizumab was a concentrate for solution for intravenous infusion, came in100mg vials as a liquid formulation for infusion and was dosed at 300mg every21 days. Spartalizumab was infused after LAG525

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

Dosage and administration details:

LAG525 was a concentrate for solution for intravenous infusion, came in100mg vials as a liquid formulation for infusion and was dosed at 400mg every21 days. For all arms, LAG525 was infused first

Arm title	LAG525+ PDR001+ carboplatin

Arm description:

Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.

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

Dosage and administration details:

LAG525 was a concentrate for solution for intravenous infusion, came in100mg vials as a liquid formulation for infusion and was dosed at 400mg every21 days. For all arms, LAG525 was infused first

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

Dosage and administration details:

Carboplatin was a concentrate for solution for intravenous infusion, came in100mg/mL and was dosed per area under the curve (AUC) 6 every 21 days. Carboplatin was infused once LAG525 infusion was completed

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

Dosage and administration details:

Spartalizumab was a concentrate for solution for intravenous infusion, came in100mg vials as a liquid formulation for infusion and was dosed at 300mg every21 days. Spartalizumab was infused after LAG525

Arm title	LAG525 + carboplatin

Arm description:

Participants received LAG525 and carboplatin administered as infusion once every 3 weeks

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

Dosage and administration details:

Carboplatin was a concentrate for solution for intravenous infusion, came in100mg/mL and was dosed per area under the curve (AUC) 6 every 21 days. Carboplatin was infused once LAG525 infusion was completed

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

Dosage and administration details:

LAG525 was a concentrate for solution for intravenous infusion, came in100mg vials as a liquid formulation for infusion and was dosed at 400mg every21 days. For all arms, LAG525 was infused first

Number of subjects in period 1	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Started	20	34	34
Treated	19	34	34
Completed	0	0	0
Not completed	20	34	34
Adverse event, serious fatal	-	-	1
Physician decision	3	6	6
Patient decision	-	1	1

Adverse event, non-fatal	2	3	3
Progressive disease	15	23	23
Terminated by sponsor (end of study definition)	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	LAG525 + PDR001
Reporting group description:	
Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	
Reporting group title	LAG525+ PDR001+ carboplatin
Reporting group description:	
Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	
Reporting group title	LAG525 + carboplatin
Reporting group description:	
Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	

Reporting group values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Number of subjects	20	34	34
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	30	28
From 65-84 years	2	4	6
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	53.8	50.9	53.3
standard deviation	± 10.22	± 10.88	± 10.78
Sex: Female, Male Units: Participants			
Female	20	34	34
Male	0	0	0
Race/Ethnicity, Customized Units: Subjects			
Asian	8	8	7
Black or African American	0	0	1
Missing	0	3	1
White	12	23	25

Reporting group values	Total		
Number of subjects	88		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	76		
From 65-84 years	12		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	88		
Male	0		
Race/Ethnicity, Customized			
Units: Subjects			
Asian	23		
Black or African American	1		
Missing	4		
White	60		

End points

End points reporting groups

Reporting group title	LAG525 + PDR001
Reporting group description:	
Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	
Reporting group title	LAG525+ PDR001+ carboplatin
Reporting group description:	
Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	
Reporting group title	LAG525 + carboplatin
Reporting group description:	
Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	

Primary: Overall response rate (ORR) per investigator’s assessment according to RECIST v1.1

End point title	Overall response rate (ORR) per investigator’s assessment according to RECIST v1.1[1]
End point description:	
Overall response rate (ORR) is defined as the percentage of participants with best overall response of complete response (CR) or partial response (PR) according to RECIST 1.1 based on investigator's assessment. The 95% CIs were computed using two-sided exact binomial method. CR: Disappearance of all non-nodal 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 approximately 14 months	

Notes:

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

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	34	34	
Units: Percentage of participants				
number (confidence interval 95%)	5.0 (0.1 to 24.9)	32.4 (17.4 to 50.5)	17.6 (6.8 to 34.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) per investigator’s assessment according to RECIST v1.1

End point title	Clinical Benefit Rate (CBR) per investigator’s assessment according to RECIST v1.1

End point description:

CBR is defined as the percentage of participants with a best overall response (BOR) of confirmed CR or PR, or stable disease (SD) lasting 24 weeks or longer, according to RECIST 1.1 criteria. The 95% CI were computed using two-sided exact binomial method.
CR: Disappearance of all non-nodal 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 approximately 14 months

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	34	34	
Units: Percentage of Participants				
number (confidence interval 95%)	5.0 (0.1 to 24.9)	35.3 (19.7 to 53.5)	20.6 (8.7 to 37.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response (TTR) per investigator's assessment according to RECIST v1.1

End point title	Time to response (TTR) per investigator's assessment according to RECIST v1.1

End point description:

TTR is the time from date of randomization to first documented response of CR or PR based on investigators' assessment and according to RECIST 1.1. Median TTR was summarized using descriptive statistics.
CR: Disappearance of all non-nodal 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 date of randomization to first documented response (CR or PR), up to approximately 14 months

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	11	6	
Units: Months				
median (full range (min-max))	1.5 (1.5 to 1.5)	1.7 (1.2 to 4.1)	1.4 (1.2 to 2.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) per investigator's assessment according to RECIST v1.1

End point title	Duration of response (DOR) per investigator's assessment according to RECIST v1.1

End point description:

DOR is the time between the first documented response (CR or PR) and the first documented progression or death due to underlying cancer based on RECIST1.1 and as per investigator's assessment. The DOR distribution was estimated using the Kaplan-Meier method and the 95% confidence intervals using the method of Brookmeyer and Crowley. If progression or death did not occur, the participant was censored at the date of last adequate tumor assessment.
CR: Disappearance of all non-nodal target lesions and 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.
Progression: at least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. The sum must also demonstrate an absolute increase of at least 5 mm.

End point type	Secondary

End point timeframe:

From first documented response up to disease progression or death due to underlying cancer, whichever occurs first, up to approximately 14 months

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	11	6	
Units: Months				
median (confidence interval 95%)	4.9 (-9999 to 9999)	13.6 (2.8 to 9999)	12.6 (2.4 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

PFS is defined as time from date of randomization to the date of first documented progression or death due to any cause. PFS was assessed via investigator's assessment according to RECIST 1.1. PFS was censored at the date of the last adequate tumor assessment if no PFS event was observed prior to the analysis cut-off date or before the start of the new anticancer therapy date, whichever is earlier. The PFS distribution was estimated using the Kaplan-Meier method. The 95% confidence intervals were calculated using the method of Brookmeyer and Crowley.

End point type	Secondary

End point timeframe:

From date of randomization to disease progression or death due to any cause, whichever occurs first, up to approximately 14 months

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	34	34	
Units: Months				
median (confidence interval 95%)	1.4 (1.2 to 1.5)	4.3 (2.8 to 5.6)	3.0 (2.2 to 5.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from date of randomization to date of death due to any cause. If a participant was not known to have died, then OS was censored at the latest date the participant was known to be alive (on or before the cut-off date). The OS distribution was estimated using the Kaplan-Meier method. The 95% confidence intervals were calculated using the method of Brookmeyer and Crowley

End point type	Secondary

End point timeframe:

From date of randomization to date of death due to any cause, up to 18 months

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	34	34	
Units: Months				
median (confidence interval 95%)	6.1 (4.6 to 9999)	11.6 (7.5 to 9999)	8.0 (6.2 to 9.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) parameter, Area under the plasma concentration versus time curve from time 0 to 504 hours (AUC0-504h) of LAG525

End point title	Pharmacokinetics (PK) parameter, Area under the plasma concentration versus time curve from time 0 to 504 hours (AUC0-504h) of LAG525

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUC0-504h was defined as the area under the plasma concentration-time curve from time zero to 504h.

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 days

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	24	33	
Units: day*microgram/miliLiter (day*ug/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 11/ 19 / 22)	1270 (± 25.8)	1350 (± 22.4)	1180 (± 23.4)	
Cycle 3 (n= 3 / 14 / 11)	2060 (± 60.1)	2200 (± 34.4)	1990 (± 31.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Cmax of LAG525

End point title	PK parameter, Cmax of LAG525

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Cmax is the maximum observed plasma LAG525 concentration

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 days

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	34	30	
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 16 / 31/ 28)	127 (± 26.5)	136 (± 21.1)	128 (± 17.9)	
Cycle 3 (n= 6 / 23 / 24)	144 (± 48.9)	181 (± 29.5)	168 (± 26.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUClast of LAG525

End point title	PK parameter, AUClast of LAG525

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUClast is the area under the curve (AUC) from time zero to the last measurable concentration sampling time (tlast) of LAG525

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 days

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	34	29	
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 16/ 31 / 28)	1170 (± 32.0)	1310 (± 41.1)	1010 (± 151.2)	
Cycle 3 (n= 6 / 23 / 24)	240 (± 9775.4)	2040 (± 49.8)	1490 (± 196.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Tmax of LAG525

End point title	PK parameter, Tmax of LAG525

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Tmax is the time to reach maximum LAG525 serum

concentration. Actual time of sample collection was used (not the nominal time point as per scheduled assessment)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 days

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	34	30	
Units: hr				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 16 / 31 / 28)	1.51 (± 13.4)	1.58 (± 15.0)	1.77 (± 37.4)	
Cycle 3 (n= 6 / 23 / 24)	1.64 (± 13.4)	1.58 (± 15.0)	1.77 (± 37.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUC0-504h of PDR001

End point title	PK parameter, AUC0-504h of PDR001[2]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUC0-504h was defined as the area under the plasma concentration-time curve from time zero to 504h.

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 days

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 only applicable for arms with PDR001 administration

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	24		
Units: day*ug/mL				
arithmetic mean (standard deviation)				
Cycle 1 (n= 11 / 18)	819 (± 23.6)	907 (± 29.1)		
Cycle 3 (n= 3 / 15)	1490 (± 41.0)	1710 (± 29.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Cmax of PDR001

End point title	PK parameter, Cmax of PDR001[3]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Cmax is the maximum observed PDR001 serum concentration

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 days

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 only applicable for arms with PDR001 administration

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	33		
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 16 / 28)	78.0 (± 18.9)	82.4 (± 25.1)		
Cycle 3 (n= 6 / 21)	95.1 (± 41.4)	117 (± 26.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUClast of PDR001

End point title	PK parameter, AUClast of PDR001[4]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUClast is the area under the curve (AUC) from time zero to the last measurable concentration sampling time (tlast) of PDR001

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 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 only applicable for arms with PDR001 administration

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	33		
Units: day*ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 16 / 28)	780 (± 24.4)	890 (± 44.6)		
Cycle 3 (n= 5 / 21)	374 (± 2703.2)	1500 (± 55.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Tmax of PDR001

End point title	PK parameter, Tmax of PDR001[5]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Tmax is the time to reach maximum PDR001 serum concentration. Actual time of sample collection was used (not the nominal time point as per scheduled assessment)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, 1 hour (hr) post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 1. Cycle 3 at pre-infusion, 1 hr post end of infusion, 168 hr, 336 hr and 504 hr post-infusion on Day 1 of Cycle 3. Each cycle is 21 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 only applicable for arms with PDR001 administration

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	33		
Units: hr				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 16 / 28)	1.43 (± 34.7)	1.71 (± 29.7)		
Cycle 3 (n= 6 / 21)	1.67 (± 13.6)	1.61 (± 13.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUC0-4h of carboplatin (total platinium)

End point title	PK parameter, AUC0-4h of carboplatin (total platinium)[6]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUC0-4h was defined as the area under the plasma concentration-time curve from time zero to 4h (determined as total platinium).

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	20		
Units: hour*nanogram/miliLiter (hr*ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 20 / 16)	45000 (± 23.0)	45200 (± 16.1)		
Cycle 3 (n= 14 / 14)	42700 (± 27.6)	43500 (± 29.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Cmax of carboplatin (total platinium)

End point title	PK parameter, Cmax of carboplatin (total platinium)[7]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Cmax is the maximum observed carboplatin plasma concentration (determined as total platinium)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 30 / 27)	22300 (± 32.0)	21400 (± 32.2)		
Cycle 3 (n = 23 / 23)	20900 (± 33.4)	20000 (± 199.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUClast of carboplatin (total platinium)

End point title	PK parameter, AUClast of carboplatin (total platinium)[8]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUClast is the area under the curve (AUC) from time zero to the last measurable concentration sampling time (tlast) of carboplatin (determined as total platinium)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	29		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 28 / 25)	42000 (± 30.8)	38900 (± 56.3)		
Cycle 3 (n= 23 / 22)	40800 (± 38.1)	42600 (± 43.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Tmax of carboplatin (total platinium)

End point title	PK parameter, Tmax of carboplatin (total platinium)[9]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Tmax is the time to reach maximum carboplatin plasma concentration (determined as total platinium). Actual time of sample collection was used (not the nominal time point as per scheduled assessment)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	31		
Units: hr				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 30 / 27)	0.857 (± 35.5)	0.720 (± 31.9)		
Cycle 3 (n=23 / 23)	0.789 (± 33.0)	0.720 (± 34.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUC0-4h of carboplatin (ultrafilterable platinium)

End point title	PK parameter, AUC0-4h of carboplatin (ultrafilterable platinium)[10]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUC0-4h was defined as the area under the plasma concentration-time curve from time zero to 4h (determined as ultrafilterable platinium).

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	7		
Units: hour*nanogram/miliLiter (hr*ng/mL)				
geometric mean (geometric coefficient of variation)				

Cycle 1 (n= 8 / 5)	43600 (± 13.1)	44700 (± 23.4)		
Cycle 3 (n= 9 / 5)	41100 (± 30.5)	41000 (± 12.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Cmax of carboplatin (ultrafilterable platinium)

End point title	PK parameter, Cmax of carboplatin (ultrafilterable platinium)[11]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Cmax is the maximum observed carboplatin plasma concentration (determined as ultrafilterable platinium)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	19		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 12 / 13)	23200 (± 19.8)	25700 (± 24.2)		
Cycle 3 (n= 12 / 12)	22300 (± 40.1)	14700 (± 4159.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, AUClast of carboplatin (ultrafilterable platinium)

End point title	PK parameter, AUClast of carboplatin (ultrafilterable

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. AUClast is the area under the curve (AUC) from time zero to the last measurable concentration sampling time (tlast) of carboplatin (determined as ultrafilterable platinium)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-

infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[12] - 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 only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 10 / 11)	41400 (± 13.0)	35600 (± 65.2)		
Cycle 3 (n= 12 / 11)	37400 (± 30.1)	36300 (± 68.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameter, Tmax of carboplatin (ultrafilterable platinium)

End point title	PK parameter, Tmax of carboplatin (ultrafilterable platinium)[13]

End point description:

Blood samples were collected at the indicated time points for PK analysis. PK parameters were calculated by standard non-compartmental analysis. Tmax is the time to reach maximum carboplatin plasma concentration (determined as ultrafilterable platinium). Actual time of sample collection was used (not the nominal time point as per scheduled assessment)

End point type	Secondary

End point timeframe:

Cycle 1 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Cycle 3 at pre-infusion, end of infusion, 1 hour, 2 hours and 3 hours post end of infusion. Each cycle is 21 days

Notes:

[13] - 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 only applicable for arms with carboplatin administration

End point values	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	19		
Units: hr				
geometric mean (geometric coefficient of variation)				
Cycle 1 (n= 12 / 13)	0.802 (± 42.5)	0.660 (± 34.4)		
Cycle 3 (n= 12 / 12)	0.828 (± 39.7)	0.686 (± 34.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Anti-drug antibodies (ADA) at baseline for LAG525

End point title	Number of participants with Anti-drug antibodies (ADA) at baseline for LAG525

End point description:

Number of participants who had an ADA positive result at baseline for LAG525

End point type	Secondary

End point timeframe:

Baseline

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	34	33	
Units: Participants	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Anti-drug antibodies (ADA) on treatment for LAG525

End point title	Number of participants with Anti-drug antibodies (ADA) on treatment for LAG525

End point description:

Number of participants who were treatment-induced ADA positive for LAG525 (post-baseline ADA positive with ADA-negative sample at baseline) and treatment-boosted ADA positive for LAG525 (post-baseline ADA positive with titer that was at least the fold titer change greater than the ADA-positive baseline titer)

End point type	Secondary

End point timeframe:

From Cycle 1 to Cycle 7 (Day 1 pre-infusion) and end of treatment, assessed up to 3 years

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	32	32	
Units: Participants	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Anti-drug antibodies (ADA) at baseline for PDR001

End point title	Number of participants with Anti-drug antibodies (ADA) at baseline for PDR001[14]

End point description:

ADA prevalence at baseline was calculated as the percentage of participants who had an ADA positive result at baseline for PDR001.

End point type	Secondary

End point timeframe:

Baseline

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable for arms with PDR001 administration

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	34		
Units: Participants	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Anti-drug antibodies (ADA) on treatment for PDR001

End point title	Number of participants with Anti-drug antibodies (ADA) on treatment for PDR001[15]

End point description:

Number of participants who were treatment-induced ADA positive for PDR001 (post-baseline ADA positive with ADA-negative sample at baseline) and treatment-boosted ADA positive for PDR001 (post-baseline ADA positive with titer that was at least the fold titer change greater than the ADA-positive baseline titer)

End point type	Secondary

End point timeframe:

From Cycle 1 to Cycle 7 (Day 1 pre-infusion) and end of treatment, assessed up to 2.8 years

Notes:

[15] - 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 only applicable for arms with PDR001 administration

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	25		
Units: Participants	1	0		

Statistical analyses

No statistical analyses for this end point

Post-hoc: All collected deaths

End point title	All collected deaths

End point description:

On-treatment deaths were collected from first dose of study medication to 30 days after the last dose of study medication for a maximum duration of 2.9 years.
Extended safety follow up deaths were collected from day 31 post treatment up to 150 days post-treatment, for a maximum duration of 3.2 years.
Post-treatment deaths were collected after 150 days post-treatment, for a maximum duration of 3.2 years.

End point type	Post-hoc

End point timeframe:

Up to 2.9 years (on-treatment), up to 3.2 years (extended safety follow-up and post-treatment)

End point values	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	19	34	34	
Units: Participants				
On-treatment	0	2	1	
Extended safety follow-up deaths	7	7	16	
Post-treatment deaths	8	15	11	
All deaths	15	24	28	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment: from first dose of study treatment until last dose of study treatment plus 30 days post treatment, up to 2.9 years.
Extended safety follow-up: from day 31 to day 150 after last administration of study treatment, up to 3.2 years

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	24.1

Reporting groups

Reporting group title	LAG525 + PDR001 (On-treatment)
Reporting group description:	
Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	
Reporting group title	LAG525 + PDR001 (Extended safety follow-up)
Reporting group description:	
Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	
Reporting group title	LAG525 + PDR001 +Carboplatin (On-treatment)
Reporting group description:	
Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks	
Reporting group title	LAG525 + PDR001 + Carboplatin (Extended safety follow-up)
Reporting group description:	
Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	
Reporting group title	LAG525 + Carboplatin (On-treatment)
Reporting group description:	
Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	
Reporting group title	LAG525 + Carboplatin (Extended safety follow-up)
Reporting group description:	
Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	

Serious adverse events	LAG525 + PDR001 (On-treatment)	LAG525 + PDR001 (Extended safety follow-up)	LAG525 + PDR001 +Carboplatin (On-treatment)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 19 (31.58%)	0 / 19 (0.00%)	12 / 34 (35.29%)
number of deaths (all causes)	0	7	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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
General physical health deterioration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Malaise			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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			
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pleuritic pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Interstitial lung disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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			
Platelet count decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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
Troponin increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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			
Thoracic vertebral fracture			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Fanconi syndrome			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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
Cardiac disorders			
Myocardial infarction			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Pericardial effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial thrombosis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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			
Brain oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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			
Anaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Febrile neutropenia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Erosive duodenitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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 ischaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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			
Biliary colic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
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 tubular acidosis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (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
Septic shock			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (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

Serious adverse events	LAG525 + PDR001 + Carboplatin (Extended safety follow-up)	LAG525 + Carboplatin (On-treatment)	LAG525 + Carboplatin (Extended safety follow-up)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 34 (17.65%)	14 / 34 (41.18%)	2 / 34 (5.88%)
number of deaths (all causes)	7	1	16
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (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 health deterioration			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Malaise			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (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
Respiratory, thoracic and mediastinal			

disorders			
Dyspnoea			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (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
Pleuritic pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Interstitial lung disease			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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			
Platelet count decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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
Troponin increased			

subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Injury, poisoning and procedural complications			
Thoracic vertebral fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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
Congenital, familial and genetic disorders			
Fanconi syndrome			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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			
Myocardial infarction			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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	1 / 34 (2.94%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Wolff-Parkinson-White syndrome			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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
Atrial thrombosis			

subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (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 disorders			
Brain oedema			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Headache			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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			
Anaemia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	1 / 34 (2.94%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Erosive duodenitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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
Faeces discoloured			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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

Intestinal ischaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Vomiting			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (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
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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 tubular acidosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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			
Back pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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 / 34 (2.94%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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
Subcutaneous abscess			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (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			
Hypercalcaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	LAG525 + PDR001 (On-treatment)	LAG525 + PDR001 (Extended safety follow-up)	LAG525 + PDR001 +Carboplatin (On-treatment)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)	0 / 19 (0.00%)	34 / 34 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to skin			

subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	11 / 34 (32.35%)
occurrences (all)	0	0	13
Chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Gait disturbance			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	11 / 34 (32.35%)
occurrences (all)	3	0	13
Chills			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	3 / 34 (8.82%)
occurrences (all)	1	0	3
Influenza like illness			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Induration			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	1	0	4
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Vaginal discharge			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Pelvic pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	7 / 34 (20.59%)
occurrences (all)	2	0	8
Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	1	0	5
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	0	0	4
Haemoptysis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Pleural effusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Psychiatric disorders			

Anxiety			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Insomnia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	6 / 34 (17.65%)
occurrences (all)	1	0	6
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	2	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	0	0	4
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	1	0	5
Platelet count decreased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	14 / 34 (41.18%)
occurrences (all)	1	0	41
Neutrophil count decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	11 / 34 (32.35%)
occurrences (all)	0	0	24
Weight decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0

SARS-CoV-2 test negative			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
White blood cell count decreased			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	0	0	8
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	2
Dysgeusia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	3
Intercostal neuralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	8 / 34 (23.53%)
occurrences (all)	2	0	10
Paraesthesia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	0	6
Anaemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	20 / 34 (58.82%)
occurrences (all)	1	0	28
Neutropenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	9 / 34 (26.47%)
occurrences (all)	0	0	16
Thrombocytopenia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	15 / 34 (44.12%)
occurrences (all)	0	0	34
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	1	0	5
Abdominal distension			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	1	0	6
Constipation			
subjects affected / exposed	3 / 19 (15.79%)	0 / 19 (0.00%)	7 / 34 (20.59%)
occurrences (all)	3	0	11
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	0	0	10
Dry mouth			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	0	0	5
Dyspepsia			

subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Dysphagia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	3 / 19 (15.79%)	0 / 19 (0.00%)	18 / 34 (52.94%)
occurrences (all)	3	0	42
Toothache			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	7 / 34 (20.59%)
occurrences (all)	0	0	12
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	3 / 34 (8.82%)
occurrences (all)	0	0	3
Dry skin			
subjects affected / exposed	3 / 19 (15.79%)	0 / 19 (0.00%)	3 / 34 (8.82%)
occurrences (all)	3	0	3
Eczema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	2
Pruritus			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	2	0	6
Rash			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	6 / 34 (17.65%)
occurrences (all)	2	0	7
Skin lesion			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0

Renal and urinary disorders			
Polyuria			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Hypothyroidism			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	0	0	5
Thyroiditis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	3 / 34 (8.82%)
occurrences (all)	1	0	5
Back pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	7 / 34 (20.59%)
occurrences (all)	1	0	8
Bone pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	2	0	2

Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	5 / 34 (14.71%)
occurrences (all)	0	0	8
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Lymphangitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	1	0	3
Skin infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	3
Urinary tract infection			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 19 (10.53%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	2	0	5
Hyperglycaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Hypocalcaemia			

subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	2 / 34 (5.88%)
occurrences (all)	0	0	2
Hypokalaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	0	0	7
Hypomagnesaemia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 19 (0.00%)	4 / 34 (11.76%)
occurrences (all)	0	0	5
Hyponatraemia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	1 / 34 (2.94%)
occurrences (all)	1	0	1
Hypophagia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 19 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	LAG525 + PDR001 + Carboplatin (Extended safety follow-up)	LAG525 + Carboplatin (On-treatment)	LAG525 + Carboplatin (Extended safety follow-up)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 34 (32.35%)	33 / 34 (97.06%)	3 / 34 (8.82%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to skin			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 34 (0.00%)	5 / 34 (14.71%)	0 / 34 (0.00%)
occurrences (all)	0	5	0
Chest pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Gait disturbance			

subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 34 (2.94%)	12 / 34 (35.29%)	0 / 34 (0.00%)
occurrences (all)	1	12	0
Chills			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Induration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	2	3	0
Pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	1 / 34 (2.94%)
occurrences (all)	0	3	1
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Vaginal discharge			

subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 34 (0.00%)	4 / 34 (11.76%)	0 / 34 (0.00%)
occurrences (all)	0	6	0
Dyspnoea			
subjects affected / exposed	0 / 34 (0.00%)	6 / 34 (17.65%)	0 / 34 (0.00%)
occurrences (all)	0	6	0
Oropharyngeal pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Haemoptysis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 34 (2.94%)	6 / 34 (17.65%)	0 / 34 (0.00%)
occurrences (all)	1	6	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 34 (2.94%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	1	2	0
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	2 / 34 (5.88%)	9 / 34 (26.47%)	0 / 34 (0.00%)
occurrences (all)	2	26	0
Neutrophil count decreased			
subjects affected / exposed	2 / 34 (5.88%)	6 / 34 (17.65%)	0 / 34 (0.00%)
occurrences (all)	2	13	0
Weight decreased			
subjects affected / exposed	3 / 34 (8.82%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	3	2	0
SARS-CoV-2 test negative			
subjects affected / exposed	1 / 34 (2.94%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
White blood cell count decreased			
subjects affected / exposed	1 / 34 (2.94%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Dizziness			
subjects affected / exposed	1 / 34 (2.94%)	6 / 34 (17.65%)	0 / 34 (0.00%)
occurrences (all)	1	8	0
Dysgeusia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Intercostal neuralgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 34 (0.00%)	4 / 34 (11.76%)	1 / 34 (2.94%)
occurrences (all)	0	5	1
Paraesthesia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	1 / 34 (2.94%)
occurrences (all)	0	1	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Somnolence			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 34 (0.00%)	5 / 34 (14.71%)	0 / 34 (0.00%)
occurrences (all)	0	11	0
Anaemia			
subjects affected / exposed	5 / 34 (14.71%)	19 / 34 (55.88%)	1 / 34 (2.94%)
occurrences (all)	7	26	1
Neutropenia			
subjects affected / exposed	1 / 34 (2.94%)	7 / 34 (20.59%)	0 / 34 (0.00%)
occurrences (all)	1	10	0
Thrombocytopenia			
subjects affected / exposed	0 / 34 (0.00%)	14 / 34 (41.18%)	1 / 34 (2.94%)
occurrences (all)	0	28	1
Eye disorders			

Dry eye			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	2	3	0
Abdominal distension			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Constipation			
subjects affected / exposed	1 / 34 (2.94%)	16 / 34 (47.06%)	0 / 34 (0.00%)
occurrences (all)	1	19	0
Diarrhoea			
subjects affected / exposed	2 / 34 (5.88%)	7 / 34 (20.59%)	0 / 34 (0.00%)
occurrences (all)	2	8	0
Dry mouth			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Dysphagia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	2 / 34 (5.88%)	13 / 34 (38.24%)	1 / 34 (2.94%)
occurrences (all)	2	17	1
Toothache			

subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 34 (2.94%)	7 / 34 (20.59%)	0 / 34 (0.00%)
occurrences (all)	4	8	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 34 (0.00%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	0	3	0
Dry skin			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 34 (2.94%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Skin lesion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Polyuria			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Thyroiditis			

subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 34 (2.94%)	4 / 34 (11.76%)	0 / 34 (0.00%)
occurrences (all)	1	5	0
Back pain			
subjects affected / exposed	2 / 34 (5.88%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	3	3	0
Bone pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 34 (5.88%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 34 (0.00%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 34 (2.94%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	1	1	0
Conjunctivitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Lymphangitis			

subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 34 (2.94%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	1 / 34 (2.94%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 34 (0.00%)	4 / 34 (11.76%)	0 / 34 (0.00%)
occurrences (all)	0	4	0
Hyperglycaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 34 (0.00%)	0 / 34 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 34 (5.88%)	2 / 34 (5.88%)	0 / 34 (0.00%)
occurrences (all)	3	2	0
Hypomagnesaemia			
subjects affected / exposed	1 / 34 (2.94%)	3 / 34 (8.82%)	0 / 34 (0.00%)
occurrences (all)	1	4	0
Hyponatraemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 34 (2.94%)	0 / 34 (0.00%)
occurrences (all)	0	1	0

Hypophagia subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	1 / 34 (2.94%) 1	0 / 34 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2018	The key purpose of this amendment was to update the protocol with the iRECIST guideline in Appendix 4, to align withdrawal of consent (WoC) language with the European Economic Area (EEA) General Data Protection Regulation (GDPR), to specify and clarify various Inclusion/Exclusion criteria, to clarify study assessments parameters related to blood samples, pregnancy, sample collections, and ECG, to clarify that patient receiving study treatment beyond progressive disease should be re-consented in a separate ICF, to extend the period to 9 months until when efficacy assessments were performed every 6 weeks, to specify an early safety review will be done after the first 8 patients enrolled in each arm have completed their first 3-week treatment cycle, etc.
05 October 2018	The purpose of this amendment was to implement Health Authority feedback as well as updates to the Novartis standard protocol language for PDR001-related protocols. An increased risk of potentially fatal autoimmune myocarditis was observed in non-Novartis clinical trials with the combination of anti-LAG-3 and PD-1 inhibitors. Therefore, measures to optimize detection of possible autoimmune myocarditis have been included. The implementation of version 5.0 of the NCI-CTCAE grading system throughout the protocol also occurred.
28 March 2019	The main purpose of this amendment was to stop enrollment to treatment Arm 1 (LAG525 + spartalizumab combination). Novartis and the study SC decided to prematurely stop enrollment of patients to Arm 1 after data review showed an increased treatment discontinuation rate due to progressive disease in Arm 1 as compared to the other two arms (both containing carboplatin).
15 February 2021	The key changes of protocol amendment 4 were to define the duration of the follow-up period and to clarify the trial discontinuation rules for participants who are still ongoing in the trial as to whether they are eligible for a Post Trial Access (PTA) program i.e. rollover protocol or a post study drug supply (PSDS).

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 999 as data points in this record are not an accurate representation of the clinical trial results.
Please use: https://www.novctrd.com complete trial results.

Notes: