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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Spartalizumab (PDR001), Ieramilimab (LAG525), capmatinib (INC280), Canakinumab ACZ885), ribociclib (LEE011)

Trial Indication(s)

Melanoma

Protocol Number

CPDR001J2201

Protocol Title

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

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: September 10, 2018 (Actual)
Primary Completion Date: December 30, 2022 (Actual)
Study Completion Date: December 30, 2022 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This study was a randomized, open-label, two-part, multi-center, open platform phase II study designed to evaluate the efficacy and safety of the anti-PD-1 antibody PDR001 in combination with novel agents for previously treated unresectable or metastatic melanoma. Additionally, a non-randomized single-arm was added based on interim analysis findings to assess the efficacy and safety of PDR001 in combination with LAG525 in subjects with previously treated unresectable or metastatic LAG-3 positive melanoma.

The study consisted of two parts: the selection part and the expansion part, which were applicable to both the randomized and non-randomized sections. In the randomized section, participants were randomized to one of four combination arms available for enrollment:

- Arm 1: LAG525 600 mg intravenously (i.v.) every 4 weeks (Q4W) and PDR001 400 mg i.v. Q4W.
- Arm 2: INC280 400 mg orally (p.o.) twice daily (BID) and PDR001 400 mg i.v. Q4W.
- Arm 3: ACZ885 300 mg subcutaneously (s.c.) every 4 weeks (Q4W) and PDR001 400 mg i.v. Q4W.
- Arm 4: LEE011 600 mg p.o. once daily (QD) on Days 1-21 of a 28-day cycle and PDR001 400 mg i.v. Q4W.

At each interim analysis, the following determinations were made: (1) which arm met the pre-specified efficacy criteria and expanded to the expansion part, (2) which arms continued enrollment in selection part (up to 45 subjects), and (3) which arms were discontinued due to futility, considering efficacy, safety, and biomarker data. The expansion phase included enrollment of subjects only in the combination arms that met the pre-specified criteria in selection part.

In the non-randomized section, a single combination arm was opened for enrollment in selection part:

- Arm 1A: LAG525 600 mg i.v. Q4W and PDR001 400 mg i.v. Q4W, assessed in a population selected based on the LAG-3 status of their tumor.

Arm 1A would be eligible for enrollment in expansion part only if it met the pre-specified criterion for this arm.

Participants received the study treatment corresponding to their assigned arm on a 28-day cycle basis until disease progression, as determined by local assessment using RECIST v1.1 criteria, or until certain events occurred, such as unacceptable toxicity, initiation of subsequent anti-cancer therapy, withdrawal of consent, investigator's decision, loss to

follow-up, death, or termination of the study by the sponsor. Following discontinuation of the study treatment, all subjects were monitored for safety evaluations for up to 150 days after their last dose of the study treatment.

Centers

31 centers in 10 countries: France(3), United States(6), Australia(2), Spain(3), Germany(5), Switzerland(1), Canada(2), United Kingdom(4), Netherlands(2), Italy(3)

Objectives:

Primary Objective:

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

Secondary Objectives:

- To evaluate the efficacy of each combination arm in terms of duration of response (DoR)
- To evaluate the efficacy of each combination arm as measured by progression-free survival (PFS) and disease control rate (DCR)
- To evaluate the overall survival (OS) of each combination arm
- To characterize the safety and tolerability of each combination arm
- To characterize the prevalence and incidence of immunogenicity of PDR001, LAG525 and ACZ885 in each combination arm
- To evaluate changes in levels and phenotype of T cell populations in the tumor and tumor microenvironment after treatment with combination therapies

Test Product (s), Dose(s), and Mode(s) of Administration

- PDR001: 400 mg of PDR001 administered every 4 weeks intravenously.
- LAG525: 600 mg of LAG525 administered every 4 weeks intravenously.
- INC280: 400 mg of INC280 administered twice daily orally.
- ACZ885: 200 mg of ACZ885 administered every 4 weeks subcutaneously.
- LEE011: 600 mg of LEE011 orally taken once daily on Days 1-21 of a 28-day cycle.

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Statistical Methods

Analysis of the primary endpoint:

- Confirmed ORR was defined as the percentage of subjects with confirmed best overall response (BOR) of complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumours (RECIST) v1.1. ORR were calculated using local investigator review of tumor assessment data and summarized using descriptive statistics (N,%) along with 2-sided exact 95% confidence interval using the Clopper-Pearson method. No formal hypothesis testing was conducted.

Analysis of the secondary endpoints:

- DoR was defined as the time from the date of first documented response of CR or PR to the date of the first documented progression or death due to underlying cancer. DoR was based on local investigators review of tumor assessments using RECIST v1.1 criteria.
- PFS was defined as the time from the date of randomization to the date of the first documented progression or death due to any cause. PFS was based on local investigator assessments using RECIST v1.1 criteria.
- DCR was defined as the percentage of patients with a BOR of confirmed CR or PR, or stable disease (SD) lasting 12 weeks or longer, according to RECIST v1.1 criteria. DCR was calculated based on the local investigator assessments.
- OS was defined as the time from date of randomization to date of death due to any cause. All deaths were used in the OS analysis. If a patient was not known to have died at the time of analysis, OS was censored at the date of last contact.
- Immunogenicity was characterized descriptively tabulating ADA prevalence at baseline and ADA incidence on-treatment.
- Changes in levels, phenotype and/or activation of T cell populations in the tumor and tumor microenvironment were analyzed. Such analyses included CD8+ T cell infiltration and T cell activation by IHC and gene expression analysis, and T cell repertoire/clonality by TCR sequencing.

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Study Population: Key Inclusion/Exclusion Criteria

Key inclusion criteria for Arm 1, 2, 3, 4:

• Histologically confirmed unresectable or metastatic stage IIIB/C/D or IV melanoma using AJCC edition 8.

• Previously treated for unresectable or metastatic melanoma:

-Subjects with V600BRAF wild-type disease had to have received prior systemic therapy for unresectable or metastatic melanoma with anti-PD-1/PD-L1. Additionally, subjects may have received anti-CTLA-4 as a single agent or in combination with anti-PD-1/PD-L1, irrespective of the sequence. No additional systemic treatment was allowed for advanced or metastatic melanoma.
A maximum of two prior lines of systemic therapies for unresectable or metastatic melanoma were allowed.
The last dose of prior therapy (anti-PD-1, anti-PD-L1, or anti-CTLA-4) had to have been received more than four weeks before randomization.

-Subjects with V600BRAF mutant disease had to have received prior systemic therapy for unresectable or metastatic melanoma with anti-PD-1/PD-L1 and V600BRAF inhibitor. Additionally, subjects may have received anti-CTLA-4 as a single agent or in combination with anti-PD-1/PD-L1, or MEK inhibitor (in combination with V600BRAF inhibitor or as a single agent), irrespective of the sequence. No additional systemic treatment was allowed for advanced or metastatic melanoma.
-A maximum of three prior lines of systemic therapies for unresectable or metastatic melanoma were allowed.
-The last dose of prior therapy had to have been received more than 4 weeks (for anti-PD-1, anti-PD-L1, or anti-CTLA-4) or more than 2 weeks (for V600BRAF or MEK inhibitor) prior to randomization.
-All subjects (with V600BRAF wild-type disease and with V600BRAF mutant disease) had to have documented disease progression as per RECIST v1.1 while on/after the last therapy received prior to study entry and while on/after treatment with anti-PD1/PD-L1. The last progression had to have occurred within 12 weeks prior to randomization in the study.

• ECOG performance status 0-2.

• At least one measurable lesion per RECIST v1.1.

• At least one lesion, suitable for sequential mandatory tumor biopsies (screening and on-treatment) in accordance with the biopsy guidelines specified in the protocol. The same lesion had to be biopsied sequentially.

• Screening tumor biopsy had to fulfill the tissue quality criteria outlined in the protocol, as assessed by a local pathologist.

Key inclusion criteria for Arm 1A:

• Histologically confirmed unresectable or metastatic stage IIIB/C/D or IV melanoma according to AJCC Edition 8.

• Previously treated for unresectable or metastatic melanoma:

-All subjects had to have received anti-PD-1 checkpoint inhibitor therapy (i.e., pembrolizumab or nivolumab) either as monotherapy or in combination with ipilimumab as the last systemic therapy prior to enrollment and had to have confirmed disease progression as per RECIST v1.1 (confirmed on a subsequent scan, which could be the scan performed during screening) while on or after this therapy prior to enrollment.
-Subjects with V600BRAF wild-type disease had to have received no more than 2 prior systemic therapies, including prior anti-PD-

1/PD-L1 (as monotherapy or in combination with ipilimumab).
-Subjects with V600BRAF mutant disease had to have received no more than 3 prior systemic therapies, including anti-PD-1/PD-L1 (as monotherapy or in combination with ipilimumab) and V600BRAF inhibitor (as monotherapy or in combination with a MEK inhibitor).
-The last dose of anti-PD-1-based therapy had to have been received more than four weeks prior to the first dose of study treatment.
-The last documented disease progression had to have occurred within 12 weeks prior to the first dose of study treatment.
-No additional systemic treatment was allowed for advanced or metastatic melanoma (this included, for example, tumor-infiltrating lymphocyte therapy).
• ECOG performance status 0-1.
• At least one measurable lesion per RECIST v1.1.
• Subjects had to have a baseline tumor sample that was positive for LAG-3 per central assessment.

Key exclusion criteria common to all combination arms:
• Subjects with uveal or mucosal melanoma.
• Presence of clinically active or unstable brain metastasis at the time of screening.
• Use of any live vaccines against infectious diseases within 3 months before randomization/enrollment.
• Active infection requiring systemic antibiotic therapy at the time of randomization/enrollment.
• Subjects with a condition requiring systemic treatment with either corticosteroids (>10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of randomization/enrollment. Inhaled or topical steroids, and adrenal replacement steroid doses >10 mg daily prednisone equivalent, were permitted in the absence of active autoimmune disease.
• Active, known or suspected autoimmune disease or a documented history of autoimmune disease.
• Prior allogenic bone marrow or solid organ transplant.
• History of known hypersensitivity to any of the investigational drugs used in this study.
• Malignant disease, other than that being treated in this study.
• Prior systemic therapy for unresectable or metastatic melanoma with any investigational agent or with any other agent except anti-PD-1/PD-L1 and anti-CTLA-4 (and V600BRAF and MEK inhibitors if the subject has V600BRAF mutant disease). Prior neoadjuvant and/or adjuvant therapy for melanoma completed less than 6 months before the start of the study treatment.
• Medical history or current diagnosis of myocarditis.
• Cardiac Troponin T (or Troponin I) level > 2 x ULN at screening.

Participant Flow Table

Overall Study

	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)	Total
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Started	45	43	43	44	21	196
Treated	45	43	42	44	21	195
Completed	0	0	0	0	0	0
Not Completed	45	43	43	44	21	196
Adverse Event	3	3	5	11	1	23
Death	2	2	3	0	1	8
Physician Decision	6	7	6	3	2	24
Progressive disease	33	28	26	30	16	133
Subject Decision	1	3	3	0	1	8

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Baseline Characteristics

	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)	Total
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	
Number of Participants [units: participants]	45	43	43	44	21	196
Baseline Analysis Population Description						
Age Categorical (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)						
<=18 years	0	0	0	0	0	0
Between 18 and 65 years	29	29	28	28	8	122
>=65 years	16	14	15	16	13	74
Sex: Female, Male (units: Participants)						

Analysis Population Type: Participants Count of Participants (Not Applicable)						
Female	17	21	15	14	9	76
Male	28	22	28	30	12	120
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)						
American Indian or Alaska Native	0	0	0	0	0	0
Asian	0	0	1	0	1	2
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0
White	45	42	38	42	20	187
More than one race	0	0	0	0	0	0
Unknown or Not Reported	0	1	4	2	0	7

Primary Outcome Result(s)

Overall Response Rate (ORR)

Description	ORR defined as the percentage of patients with a best overall response of either confirmed complete response (CR) or partial response (PR) as per local review by Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) and assessed by computed tomography (CT)/ magnetic resonance imaging (MRI). CR:Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to 49 months (randomized section) and 18 months (non-randomized section)
Analysis Population Description	Randomized section: All participants to whom study treatment was assigned by randomization. Non-randomized section: All participants who received at least one dose of study treatment

	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	45	43	43	44	21
Overall Response Rate (ORR) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	8.9 (2.5 to 21.2)	4.7 (0.6 to 15.8)	4.7 (0.6 to 15.8)	6.8 (1.4 to 18.7)	14.3 (3.0 to 36.3)

Secondary Outcome Result(s)

Duration of Response (DOR)

Description DOR defined as the time from date of first documented CR or PR to date of first documented disease progression (as per local review by RECIST v1.1 and assessed by CT/MRI) or death due to any cause. Subjects continuing without progression or death due to underlying cancer were censored at the date of their last adequate tumor assessment. CR:Disappearance of all non-nodal target and non-target lesions.

	In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	From first documented response to disease progression or death due to any cause, whichever occurs first, assessed up to 49 months (randomized part) and 18 months (non-randomized part)
Analysis Population Description	Randomized section: All participants to whom study treatment was assigned by randomization for whom best overall response was complete response or partial response. Non-randomized section: All participants who received at least one dose of study treatment for whom best overall response was complete response or partial response

	Arm 1: LAG525 + PDR001 (randomized section)	**Arm 2: INC280+PDR001 (randomized section)**	**Arm 3: ACZ885 + PDR001 (randomized section)**	**Arm 4: LEE011 + PDR001 (randomized section)**	**Arm 1A: LAG525 + PDR001 (non-randomized section)**
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	4	2	2	3	3
Duration of Response (DOR) (units: Days)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	476 (169 to 1373)	941.5 (504 to 1379)	617.5 (113 to 1122)	217 (169 to 281)	281 (169 to 449)

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Overall Survival (OS)

Description	OS was defined as the time from date of randomization (or date of first dose of study treatment in non-randomized part) to date of death due to any cause. The OS distribution was estimated using the Kaplan-Meier method, and the medians and 95% confidence intervals of the medians were presented.
Time Frame	From randomization (or start of treatment for non-randomized section) to death due to any cause, assessed up to 49 months (randomized section) and 24 months (non-randomized section)
Analysis Population Description	Randomized section: All participants to whom study treatment was assigned by randomization. Non-randomized section: All participants who received at least one dose of study treatment

	Arm 1: LAG525 + PDR001 (randomized section)	**Arm 2: INC280+PDR001 (randomized section)**	**Arm 3: ACZ885 + PDR001 (randomized section)**	**Arm 4: LEE011 + PDR001 (randomized section)**	**Arm 1A: LAG525 + PDR001 (non-randomized section)**
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	45	43	43	44	21
Overall Survival (OS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	8.8 (6.3 to 21.4)	12.1 (6.6 to 18.5)	8.7 (5.7 to 17.9)	10.1 (7.4 to 15.6)	14.0 (8.4 to NA)[1]

[1] NA: Not estimable due to the insufficient number of participants with events

Progression Free Survival (PFS)

Description	PFS was defined as the time between the date of randomization (or date of first dose of study treatment in non-randomized section) to the date of event defined as the first documented disease progression (as per local review by RECIST v1.1 and assessed by CT/MRI) or death due to any cause. If a subject had not had an event before leaving study or initiation of subsequent anticancer therapy, PFS was censored at the date of last adequate tumor assessment. The PFS distribution was estimated using the Kaplan-Meier method, medians and 95% confidence interval of the medians were presented.
Time Frame	From randomization (or start of treatment for non-randomized section) to disease progression or death due to any cause, whichever occurs first, assessed up to 49 months (randomized section) and 18 months (non-randomized section)
Analysis Population Description	Randomized section: All participants to whom study treatment was assigned by randomization. Non-randomized section: All participants who received at least one dose of study treatment

	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	45	43	43	44	21

Progression Free Survival (PFS) (units: Months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	2.7 (1.7 to 2.8)	2.7 (2.4 to 2.8)	2.7 (2.6 to 2.8)	2.8 (2.7 to 4.4)	2.8 (2.7 to 4.6)

Disease Control Rate (DCR)

Description	DCR was defined as the percentage of participants with best overall response of CR, PR or stable disease (SD) (as per local review by RECIST v1.1 and assessed by CT/MRI). CR:Disappearance of all non-nodal target and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.
Time Frame	Up to 49 months (randomized section) and 18 months (non-randomized section)
Analysis Population Description	Randomized section: All participants to whom study treatment was assigned by randomization. Non-randomized section: All participants who received at least one dose of study treatment

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

Number of Participants Analyzed [units: participants]	45	43	43	44	21
Disease Control Rate (DCR) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	15.6 (6.5 to 29.5)	16.3 (6.8 to 30.7)	18.6 (8.4 to 33.4)	31.8 (18.6 to 47.6)	33.3 (14.6 to 57.0)

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

Description	Percentage of participants who had a PDR001 ADA positive result at baseline.
Time Frame	At Baseline
Analysis Population Description	Randomized section: Participants to whom study treatment was assigned by randomization with a determinant baseline immunogenicity sample for PDR001. Non-randomized section: Participants who received at least one dose of treatment with a determinant baseline immunogenicity sample for PDR001.

	Arm 1: LAG525 + PDR001 (randomized section)	**Arm 2: INC280+PDR001 (randomized section)**	**Arm 3: ACZ885 + PDR001 (randomized section)**	**Arm 4: LEE011 + PDR001 (randomized section)**	**Arm 1A: LAG525 + PDR001 (non-randomized section)**
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	43	38	40	41	20

Percentage of participants with PDR001 Anti-drug antibodies (ADA) positive result at baseline (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	1 (2.33%)	0 (%)	1 (2.5%)	0 (%)	0 (%)

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

Description	Percentage of participants who had a LAG525 ADA positive result at baseline. Only applicable for participants enrolled in Arm 1 and Arm 1A.
Time Frame	At Baseline
Analysis Population Description	Randomized section: Participants randomized to Arm 1 with a determinant baseline immunogenicity sample for LAG525. Non-randomized section: Participants who received at least one dose of treatment with a determinant baseline immunogenicity sample for LAG525.

	Arm 1: LAG525 + PDR001 (randomized section)	**Arm 1A: LAG525 + PDR001 (non-randomized section)**
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	43	20
Percentage of participants with LAG525 Anti-drug antibodies (ADA) positive result at baseline (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	3 (6.98%)	0 (%)

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

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

Time Frame	At Baseline
Analysis Population Description	Participants randomized to Arm 3 with a determinant baseline immunogenicity sample for ACZ885.

	Arm 3: ACZ885 + PDR001 (randomized section)
Arm/Group Description	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	39
Percentage of participants with ACZ885 Anti-drug antibodies (ADA) positive result at baseline (units: Participants)	**Count of Participants (Not Applicable)**
	0 (%)

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

Description	Percentage of participants who tested positive for treatment-induced ADA for PDR001 (subjects with ADA-negative sample at baseline with at least one post-baseline ADA positive sample) as well as treatment-boosted ADA for PDR001 (subjects with baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment).
Time Frame	Pre-infusion on Day 1 of Cycle 1, 2, 3, 4, 5, 6 and thereafter every 3 cycles until end of treatment (EOT), EOT, and 30 and 150 days post-EOT (assessed up to 49 months randomized section and 24 months non-randomized section). Cycle= 28 days
Analysis Population Description	Randomized section: Participants to whom study treatment was assigned by randomization with a determinant baseline immunogenicity sample and at least one determinant post-baseline immunogenicity sample. Non-randomized section: Participants who received at least one dose of study treatment with a determinant baseline immunogenicity sample and at least one determinant post-baseline immunogenicity sample.

	Arm 1: LAG525 + PDR001 (randomized section)	Arm 2: INC280+PDR001 (randomized section)	Arm 3: ACZ885 + PDR001 (randomized section)	Arm 4: LEE011 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	40	34	38	39	19
Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for PDR001 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	3 (7.5%)	5 (14.71%)	3 (7.89%)	0 (%)	0 (%)

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

Description	Percentage of participants who tested positive for treatment-induced ADA for LAG525 (subjects with ADA-negative sample at baseline with at least one post-baseline ADA positive sample) as well as treatment-boosted ADA for LAG525 (subjects with baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment). Only applicable for subjects enrolled in Arm 1 and Arm 1A.
Time Frame	Pre-infusion on Day 1 of Cycle 1, 2, 3, 4, 5, 6 and thereafter every 3 cycles until end of treatment (EOT) and EOT (assessed up to 49 months in the randomized section and 18 months in the non-randomized section). Cycle= 28 days

Analysis Population Description	Randomized section: Participants randomized to Arm 1 with a determinant baseline immunogenicity sample and at least one determinant post-baseline immunogenicity sample. Non-randomized section: Participants who received at least one dose of study treatment with a determinant baseline immunogenicity sample and at least one determinant post-baseline immunogenicity sample.

	Arm 1: LAG525 + PDR001 (randomized section)	Arm 1A: LAG525 + PDR001 (non-randomized section)
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	40	19
Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for LAG525 (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	7 (17.5%)	2 (10.53%)

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

Description	Percentage of participants who tested positive for treatment-induced ADA for ACZ885 (subjects with ADA-negative sample at baseline with at least one post-baseline ADA positive sample) as well as treatment-boosted ADA for ACZ885 (subjects with baseline positive ADA titre that was boosted to a 4-fold or higher-level following treatment). Only applicable for subjects enrolled in Arm 3.
Time Frame	Pre-infusion on Day 1 of Cycle 1, 2, 3, 4, 5, 6 and thereafter every 3 cycles until end of treatment (EOT) and EOT (assessed up to 40 months). Cycle= 28 days
Analysis Population Description	Participants randomized to Arm 3 with a determinant baseline immunogenicity sample and at least one determinant post-baseline immunogenicity sample.

	Arm 3: ACZ885 + PDR001 (randomized section)

Arm/Group Description	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	38
Percentage of participants who were treatment-induced ADA positive and treatment-boosted ADA positive for ACZ885 (units: Participants)	**Count of Participants (Not Applicable)**
	1 (2.63%)

Percentage of participants with a favorable biomarker profile (pFBP)

Description	Biomarker parameters included: 1) number of tumor infiltrating T cells (TIL), 2) activation level of TIL, and 3) changes in immune response gene expression signatures. For the number of TILs, an increase in tumoral CD8+ cell numbers compared to baseline was considered favorable. The activation level of TIL was assessed by the percentage of tumoral CD8+ cells expressing GzmB (a marker for cytotoxic activity) or Ki67 (a marker for cell proliferation), where an increase in either GZMB+/CD8+ or KI67+/CD8+ post-baseline was considered favorable. Changes in immune response gene expression signatures were evaluated by the levels in T-cell inflamed signature (TIS), where an increase from baseline was considered favorable. To be categorized as having a pFBP, a subject must meet the favorable criteria for at least two of the three biomarker parameters. The percentage of participants with pFBP was assessed.
Time Frame	Baseline and after 3-4 weeks of treatment
Analysis Population Description	Participants who received at least one dose of treatment with an evaluable baseline tumor biopsy sample and at least one evaluable post-baseline tumor biopsy sample with evaluable results for the three biomarker parameters.

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

	4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	400 mg administered intravenously every 4 weeks	4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	22	21	31	6	0
Percentage of participants with a favorable biomarker profile (pFBP) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	13.6 (2.9 to 34.9)	4.8 (0.1 to 23.8)	6.5 (0.8 to 21.4)	16.7 (0.4 to 64.1)	

Post-Hoc Outcome Result(s)

All collected deaths

Description	Pre-treatment: Deaths collected from day of patient's informed consent to the day before the first administration of study treatment. On-treatment: deaths collected from start of treatment to 30 days after last dose of study treatment. Extended safety follow-up: Deaths collected from 31 days after last dose of study treatment up to 150 days after last dose of PDR001 (if this timepoint was later than 30 days after last dose of study treatment) Post-treatment survival follow-up: Deaths collected from day 151 post-last dose of PDR001 or 31 days after last dose of study treatment (whichever occurred last) up to end of study.
Time Frame	Pre-treatment: up to 28/35 days (randomized/non-randomized). On-treatment: up to 49/19 months (randomized/non-randomized). Extended safety FU and Post-treatment survival FU: up to 49/24 months (randomized/non-randomized).
Analysis Population Description	Randomized section: All participants to whom study treatment was assigned by randomization. Non-randomized section: All participants who received at least one dose of study treatment

	Arm 1: LAG525 + PDR001	**Arm 2: INC280+PDR001 (randomized section)**	**Arm 3: ACZ885 + PDR001**	**Arm 4: LEE011 + PDR001**	**Arm 1A: LAG525 + PDR001 (non-**

	(randomized section)		(randomized section)	(randomized section)	randomized section)
Arm/Group Description	Participants randomized to receive LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive INC280 orally at a dosage of 400 mg twice daily, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive ACZ885 at a dosage of 300 mg administered subcutaneously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	Participants randomized to receive LEE011 orally at a dosage of 600 mg once daily on Days 1-21 of a 28-day cycle, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks	LAG-3 positive participants received LAG525 at a dosage of 600 mg administered intravenously every 4 weeks, in combination with PDR001 at a dosage of 400 mg administered intravenously every 4 weeks
Number of Participants Analyzed [units: participants]	45	43	43	44	21
All collected deaths (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Pre-treatment deaths	0	0	0	0	0
On-treatment deaths	5	3	3	3	1
Extended safety follow-up deaths	14	11	15	11	4
Post-treatment survival follow-up deaths	18	19	15	19	7
All deaths	37	33	33	33	12

Safety Results

Time Frame On-treatment: from first dose to 30 days post-treatment, up to 49/24 months (randomized/non-randomized) Extended safety follow-up: from 31 days after last dose of treatment up to 150 days after last dose of PDR001 (if >30 days post-treatment), up to 49/24 months

	(randomized/non-randomized) Post-treatment survival follow-up: from day 151 after last dose of PDR001 or 31 days post-treatment (whichever occurred last) up to end of study, up to 49/24 months (randomized/non-randomized).
Additional Description	Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Deaths in the post treatment survival follow-up are not considered AEs. The total number at risk in the post treatment survival includes patients that entered the post treatment survival follow-up period. Safety analyses were performed in the safety set, including all participants who received at least one dose of treatment
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Arm 1: LAG525 + PDR001 (randomized part)-on-treatment period N = 45	Arm 1: LAG525 + PDR001 (randomized part)-extended safety follow-up N = 45	Arm 1: LAG525 + PDR001 (randomized part)-post-treatment survival follow-up N = 26	Arm 2: INC280+ PDR001 (randomized part)-on-treatment period N = 43	Arm 2: INC280+ PDR001 (randomized part) - extended safety follow-up N = 43	Arm 2: INC280+ PDR001 (randomized part)-post-treatment survival follow-up N = 29	Arm 3: ACZ885 + PDR001 (randomized part)-on-treatment period N = 42	Arm 3: ACZ885 + PDR001 (randomized part)-extended safety follow-up N = 42	Arm 3: ACZ885 + PDR001 (randomized part)-post-treatment survival follow-up N = 24	Arm 4: LEE011 + PDR001 (randomized part)-on-treatment period N = 44	Arm 4: LEE011 + PDR001 (randomized part)-extended safety follow-up N = 44	Arm 4: LEE011 + PDR001 (randomized part)-post-treatment survival follow-up N = 30	Arm 1A: LAG525 + PDR001 (non-randomized part)-on-treatment period N = 21	Arm 1A: LAG525 + PDR001 (non-randomized part)-extended safety follow-up N = 21	Arm 1A: LAG525 + PDR001 (non-randomized part)-post-treatment survival follow-up N = 14
Arm/ Group	AEs collected during	AEs collected during	Deaths collected in	AEs collected during on-	AEs collected during extended	Deaths collected in the post-	AEs collected during	AEs collected during	Deaths collected in	AEs collected during	AEs collected during	Deaths collected in	AEs collected during	AEs collected during	Deaths collected in

Description	on-treatment period (up to 30 days post-treatment)	extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	treatment period (up to 30 days post-treatment)	safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	on-treatment period (up to 30 days post-treatment)	extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	on-treatment period (up to 30 days post-treatment)	extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	on-treatment period (up to 30 days post-treatment)	extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period
Total Number Affected	5	14	18	3	11	19	3	15	15	3	11	19	1	4	7
Total Number At Risk	45	45	26	43	43	29	42	42	24	44	44	30	21	21	14

Serious Adverse Events

Time Frame	On-treatment: from first dose to 30 days post-treatment, up to 49/24 months (randomized/non-randomized) Extended safety follow-up: from 31 days after last dose of treatment up to 150 days after last dose of PDR001 (if >30 days post-treatment), up to 49/24 months (randomized/non-randomized) Post-treatment survival follow-up: from day 151 after last dose of PDR001 or 31 days post-treatment (whichever occurred last) up to end of study, up to 49/24 months (randomized/non-randomized).
Additional Description	Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Deaths in the post treatment survival follow-up are not considered AEs. The total number at risk in the post treatment survival includes patients that entered the post treatment survival follow-up period. Safety analyses were performed in the safety set, including all participants who received at least one dose of treatment
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

	Arm 1: LAG525 + PDR001 (randomized part)-on-treatment period N = 45	**Arm 1: LAG525 + PDR001 (randomized part)-extended safety follow-up N = 45**	**Arm 1: LAG525 + PDR001 (randomized part)-post-treatment survival follow-up N = 0**	**Arm 2: INC280 +PDR001 (randomized part)-on-treatment period N = 43**	**Arm 2: INC280 +PDR001 (randomized part) - extended safety follow-up N = 43**	**Arm 2: INC280 +PDR001 (randomized part)-post-treatment survival follow-up N = 0**	**Arm 3: ACZ885 + PDR001 (randomized part)-on-treatment period N = 42**	**Arm 3: ACZ885 + PDR001 (randomized part)-extended safety follow-up N = 42**	**Arm 3: ACZ885 + PDR001 (randomized part)-post-treatment survival follow-up N = 0**	**Arm 4: LEE011 + PDR001 (randomized part)-on-treatment period N = 44**	**Arm 4: LEE011 + PDR001 (randomized part)-extended safety follow-up N = 44**	**Arm 4: LEE011 + PDR001 (randomized part)-post-treatment survival follow-up N = 0**	**Arm 1A: LAG525 + PDR001 (non-randomized part)-on-treatment period N = 21**	**Arm 1A: LAG525 + PDR001 (non-randomized part)-extended safety follow-up N = 21**	**Arm 1A: LAG525 + PDR001 (non-randomized part)-post-treatment survival follow-up N = 0**
Arm/Group Description	AEs collected	AEs collected	Deaths collect	AEs collected during	AEs collected during	Deaths collected in the	AEs collected	AEs collected	Deaths collect	AEs collected	AEs collected	Deaths collect	AEs collected	AEs collected	Deaths collec

	during on-treatment period (up to 30 days post-treatment)	during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	ed in the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	on-treatment period (up to 30 days post-treatment)	extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	during on-treatment period (up to 30 days post-treatment)	during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	ed in the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	during on-treatment period (up to 30 days post-treatment)	during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	ed in the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period	during on-treatment period (up to 30 days post-treatment)	during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30 days post-treatment])	ted in the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during this period
Total # Affected by any Serious Adverse Event	21	5	0	21	0	0	12	4	0	22	8	0	7	2	0
Total # at Risk by any Serious Adverse Event	45	45	0	43	43	0	42	42	0	44	44	0	21	21	0
Blood and lymphatic															

system disorders									
Anaemia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Febrile neutropenia	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Cardiac disorders									
Acute myocardial infarction	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Atrial fibrillation	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Myocarditis	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Endocrine disorders									
Adrenal haematoma	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hypercalcaemia of malignancy	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)
Gastrointestinal disorders									
Abdominal pain	0 (0.0 0%)	0 (0.0 0%)	2 (4.65 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Autoimmune colitis	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Diarrhoea	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	1 (2.3 8%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Dysphagia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)	0 (0.0 0%)
Gastritis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	2 (4.5 5%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Gastrointestinal haemorrhage	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Gastrooesophageal reflux disease	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Immune-mediated enterocolitis	0 (0.0 0%)	1 (2.2 2%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)	0 (0.0 0%)
Intestinal obstruction	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Intussusception	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Lower gastrointestinal haemorrhage	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Nausea	2 (4.4 4%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Small intestinal obstruction	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)	0 (0.0 0%)
Subileus	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)	0 (0.0 0%)
Vomiting	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

General disorders and administration site conditions									
Asthenia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Chest pain	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Fatigue	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
General physical health deterioration	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Heteroplasia	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Multiple organ dysfunction syndrome	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Oedema peripheral	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
Pain	0 (0.0 0%)	1 (2.2 2%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Pyrexia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	2 (4.5 5%)	2 (4.5 5%)	0 (0.0 0%)	0 (0.0 0%)
Hepatobiliary disorders									
Cholangitis	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Drug-induced liver injury	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hepatic cytolysis	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hepatitis	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hepatitis acute	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hypertransaminasaemia	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Immune-mediated hepatitis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	2 (4.5 5%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Immune system disorders										
Cytokine release syndrome	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Drug hypersensitivity	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Infections and infestations										
Cellulitis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Erysipelas	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Infection	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Pneumonia	0 (0.0 0%)	2 (4.4 4%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Pneumonia bacterial	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Respiratory tract infection	0 (0.0 0%)	1 (2.2 2%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Sepsis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Skin infection	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Suspected COVID-19	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
Injury, poisoning and procedural complications										
Femur fracture	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Humerus fracture	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Ocular procedural complication	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Investigations										
Blood lactic acid increased	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
General physical	2 (4.4 4%)	1 (2.2 2%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

condition abnormal										
Haemoglobin decreased	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Liver function test abnormal	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
Liver function test increased	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Metabolism and nutrition disorders										
Cachexia	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Decreased appetite	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Dehydration	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Diabetes mellitus	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
Hypoalbuminaemia	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hypokalaemia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hyponatraemia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)
Musculoskeletal and connective										

tissue disorders										
Arthralgia	1 (2.2 2%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Back pain	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Myositis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Pain in extremity	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	2 (4.5 5%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
Pathological fracture	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	2 (9.5 2%)	0 (0.0 0%)
Rhabdomyolysis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)										
Acute myeloid leukaemia	0 (0.0 0%)	1 (2.2 2%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Basal cell carcinoma	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Breast neoplasm	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Malignant neoplasm progression	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)
Metastases to bone	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Metastases to central nervous system	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Metastases to spleen	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Oncologic complication	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	1 (4.7 6%)	0 (0.0 0%)
Transitional cell carcinoma	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Tumour haemorrhage	2 (4.4 4%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Tumour pain	1 (2.2 2%)	1 (2.2 2%)	1 (2.33 %)	0 (0.00 %)	2 (4.7 6%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Nervous system disorders										
Cerebral haemorrhage	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Diabetic hyperglycaemic coma	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Dizziness	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Epilepsy	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Facial paresis	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Haemorrhage intracranial	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Headache	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hemiparesis	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hypoglossal nerve disorder	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Nervous system disorder	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Peripheral nerve paresis	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Seizure	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Spinal cord compression	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	1 (4.7 6%)	0 (0.0 0%)
Product issues										
Device dislocation	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Renal and urinary disorders										
Acute kidney injury	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Renal failure	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Reproductive system and breast disorders												
Pelvic pain	0 (0.0 0%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		0 (0.0 0%)	0 (0.0 0%)	
1 (4.7 6%)	0 (0.0 0%)											
Respiratory, thoracic and mediastinal disorders												
Acute respiratory failure	0 (0.0 0%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		0 (0.0 0%)	0 (0.0 0%)	
1 (4.7 6%)	0 (0.0 0%)											
Chronic obstructive pulmonary disease	1 (2.2 2%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		0 (0.0 0%)	0 (0.0 0%)	
0 (0.0 0%)	0 (0.0 0%)											
Dyspnoea	0 (0.0 0%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		1 (2.3 8%)	0 (0.0 0%)		0 (0.0 0%)	0 (0.0 0%)	
0 (0.0 0%)	0 (0.0 0%)											
Haemothorax	0 (0.0 0%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		0 (0.0 0%)	1 (2.2 7%)	
0 (0.0 0%)	0 (0.0 0%)											
Pleural effusion	1 (2.2 2%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		1 (2.2 7%)	0 (0.0 0%)	
0 (0.0 0%)	0 (0.0 0%)											
Pulmonary embolism	1 (2.2 2%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		1 (2.2 7%)	0 (0.0 0%)	
0 (0.0 0%)	0 (0.0 0%)											
Skin and subcutaneous tissue disorders												
Rash	0 (0.0 0%)	0 (0.0 0%)		1 (2.33 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		0 (0.0 0%)	0 (0.0 0%)	
0 (0.0 0%)	0 (0.0 0%)											
Vascular disorders												

Deep vein thrombosis	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Hypotension	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	1 (2.2 7%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Peripheral ischaemia	0 (0.0 0%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	1 (2.3 8%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Phlebitis	1 (2.2 2%)	0 (0.0 0%)	0 (0.00 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Vena cava thrombosis	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)
Venous thrombosis	0 (0.0 0%)	0 (0.0 0%)	1 (2.33 %)	0 (0.00 %)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)	0 (0.0 0%)

Other (Not Including Serious) Adverse Events

Time Frame	On-treatment: from first dose to 30 days post-treatment, up to 49/24 months (randomized/non-randomized) Extended safety follow-up: from 31 days after last dose of treatment up to 150 days after last dose of PDR001 (if >30 days post-treatment), up to 49/24 months (randomized/non-randomized) Post-treatment survival follow-up: from day 151 after last dose of PDR001 or 31 days post-treatment (whichever occurred last) up to end of study, up to 49/24 months (randomized/non-randomized).
Additional Description	Any sign or symptom that occurs during the conduct of the trial and safety follow-up. Deaths in the post treatment survival follow-up are not considered AEs. The total number at risk in the post treatment survival includes patients that entered the post treatment survival follow-up period. Safety analyses were performed in the safety set, including all participants who received at least one dose of treatment
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 5%

	Arm 1: LAG525 + PDR001 (randomized part)-on-treatment period N = 45	Arm 1: LAG525 + PDR001 (randomized part)-extended safety follow-up N = 45	Arm 1: LAG525 + PDR001 (randomized part)-post-treatment survival follow-up N = 0	Arm 2: INC280 +PDR001 (randomized part)-on-treatment period N = 43	Arm 2: INC280 +PDR001 (randomized part) - extended safety follow-up N = 43	Arm 2: INC280 +PDR001 (randomized part)-post-treatment survival follow-up N = 0	Arm 3: ACZ885 + PDR001 (randomized part)-on-treatment period N = 42	Arm 3: ACZ885 + PDR001 (randomized part)-extended safety follow-up N = 42	Arm 3: ACZ885 + PDR001 (randomized part)-post-treatment survival follow-up N = 0	Arm 4: LEE011 + PDR001 (randomized part)-on-treatment period N = 44	Arm 4: LEE011 + PDR001 (randomized part)-extended safety follow-up N = 44	Arm 4: LEE011 + PDR001 (randomized part)-post-treatment survival follow-up N = 0	Arm 1A: LAG525 + PDR001 (non-randomized part)-on-treatment period N = 21	Arm 1A: LAG525 + PDR001 (non-randomized part)-extended safety follow-up N = 21	Arm 1A: LAG525 + PDR001 (non-randomized part)-post-treatment survival follow-up N = 0
Arm/Group Description	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last	Deaths collected in the post-treatment survival follow-up period (starting from day 151 post-	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last dose of PDR001 [if >30	Deaths collected in the post-treatment survival follow-up period (starting from day 151 post-treatment). No AEs were collected during	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last	Deaths collected in the post-treatment survival follow-up period (starting from day 151 post-	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post last	Deaths collected in the post-treatment survival follow-up period (starting from day 151 post-	AEs collected during on-treatment period (up to 30 days post-treatment)	AEs collected during extended safety follow-up period (from day 31 post-treatment up to 150 days post	Deaths collected in the post-treatment survival follow-up period (starting from day 151 post-

		dose of PDR001 [if >30 days post-treatment])	treatment). No AEs were collected during this period		days post-treatment])	this period		dose of PDR001 [if >30 days post-treatment])	treatment). No AEs were collected during this period		dose of PDR001 [if >30 days post-treatment])	treatment). No AEs were collected during this period		last dose of PDR001 [if >30 days post-treatment])	treatment). No AEs were collected during this period
Total # Affected by any Other Adverse Event	40	5	0	42	6	0	32	5	0	44	9	0	18	2	0
Total # at Risk by any Other Adverse Event	45	45	0	43	43	0	42	42	0	44	44	0	21	21	0
Blood and lymphatic system disorders															
Anaemia	3 (6.67%)	2 (4.44%)		6 (13.95%)	1 (2.33%)		6 (14.29%)	1 (2.38%)		11 (25.00%)	0 (0.0%)		3 (14.29%)	1 (4.76%)	
Eosinophilia	1 (2.22%)	0 (0.0%)		0 (0.00%)	0 (0.00%)		3 (7.14%)	0 (0.0%)		0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Leukopenia	2 (4.44%)	0 (0.0%)		0 (0.00%)	0 (0.00%)		1 (2.38%)	1 (2.38%)		4 (9.09%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Lymphopenia	2 (4.44%)	1 (2.22%)		2 (4.65%)	0 (0.00%)		1 (2.38%)	0 (0.0%)		7 (15.91%)	0 (0.0%)		1 (4.76%)	0 (0.0%)	
Neutropenia	3 (6.67%)	1 (2.22%)		0 (0.00%)	0 (0.00%)		1 (2.38%)	0 (0.0%)		20 (45.45%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	

Thrombocytopenia	1 (2.22%)	1 (2.22%)	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endocrine disorders										
Hypothyroidism	2 (4.44%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Gastrointestinal disorders										
Abdominal pain	5 (11.11%)	1 (2.22%)	3 (6.98%)	0 (0.00%)	5 (11.90%)	0 (0.00%)	5 (11.36%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Constipation	8 (17.78%)	0 (0.00%)	6 (13.95%)	1 (2.33%)	7 (16.67%)	0 (0.00%)	3 (6.82%)	1 (2.27%)	0 (0.00%)	0 (0.00%)
Diarrhoea	6 (13.33%)	0 (0.00%)	10 (23.26%)	1 (2.33%)	3 (7.14%)	0 (0.00%)	9 (20.45%)	1 (2.27%)	5 (23.81%)	0 (0.00%)
Dry mouth	3 (6.67%)	0 (0.00%)	1 (2.33%)	0 (0.00%)	4 (9.52%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	1 (4.76%)	0 (0.00%)
Nausea	13 (28.89%)	0 (0.00%)	18 (41.86%)	0 (0.00%)	9 (21.43%)	1 (2.38%)	15 (34.09%)	2 (4.55%)	6 (28.57%)	0 (0.00%)
Vomiting	6 (13.33%)	0 (0.00%)	11 (25.58%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	8 (18.18%)	1 (2.27%)	3 (14.29%)	0 (0.00%)
General disorders and administration site conditions										
Asthenia	9 (20.00%)	1 (2.22%)	7 (16.28%)	1 (2.33%)	7 (16.67%)	0 (0.00%)	8 (18.18%)	2 (4.55%)	7 (33.33%)	0 (0.00%)
Chest pain	2 (4.44%)	0 (0.00%)	3 (6.98%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Chills	1 (2.22%)	0 (0.00%)	3 (6.98%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	1 (4.76%)	0 (0.00%)
Fatigue	7 (15.56%)	1 (2.22%)	5 (11.63%)	0 (0.00%)	5 (11.90%)	1 (2.38%)	8 (18.18%)	1 (2.27%)	4 (19.05%)	0 (0.00%)
Oedema peripheral	3 (6.67%)	0 (0.00%)	10 (23.26%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	1 (4.76%)	0 (0.00%)
Pain	4 (8.89%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	0 (0.00%)
Pyrexia	3 (6.67%)	0 (0.00%)	13 (30.23%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	8 (18.18%)	2 (4.55%)	2 (9.52%)	0 (0.00%)
Hepatobiliary disorders										
Hepatic cytolysis	0 (0.00%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations										
Rhinitis	3 (6.67%)	0 (0.00%)	3 (6.98%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	1 (2.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations										
Alanine aminotransferase increased	1 (2.22%)	0 (0.00%)	6 (13.95%)	0 (0.00%)	2 (4.76%)	1 (2.38%)	15 (34.09%)	2 (4.55%)	1 (4.76%)	0 (0.00%)
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	3 (6.82%)	1 (2.27%)	1 (4.76%)	0 (0.00%)
Aspartate	1 (2.22%)	0 (0.00%)	5 (11.63%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	17 (38.64%)	1 (2.27%)	1 (4.76%)	0 (0.00%)

aminotransferase increased										
Blood alkaline phosphatase increased	4 (8.89%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	5 (11.63%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	4 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood lactate dehydrogenase increased	3 (6.67%)	2 (4.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood potassium decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gamma-glutamyltransferase increased	2 (4.44%)	1 (2.22%)	2 (4.65%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	3 (6.82%)	1 (2.27%)	0 (0.00%)	0 (0.00%)

Haemoglobin decreased	1 (2.22%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (9.52%)	1 (4.76%)
Lipase increased	3 (6.67%)	1 (2.22%)	3 (6.98%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	5 (11.36%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	2 (4.44%)	0 (0.00%)	3 (6.98%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
SARS-CoV-2 test negative	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (9.09%)	1 (2.27%)	0 (0.00%)	0 (0.00%)
Weight decreased	6 (13.33%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	5 (11.90%)	1 (2.38%)	4 (9.09%)	2 (4.55%)	0 (0.00%)	0 (0.00%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders										
Decreased appetite	10 (22.22%)	0 (0.00%)	3 (6.98%)	1 (2.33%)	7 (16.67%)	0 (0.00%)	9 (20.45%)	2 (4.55%)	2 (9.52%)	0 (0.00%)

Hypoalbuminaemia	1 (2.22%)	0 (0.00%)	3 (6.98%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders										
Arthralgia	5 (11.11%)	1 (2.22%)	2 (4.65%)	1 (2.33%)	2 (4.76%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	5 (11.11%)	0 (0.00%)	4 (9.30%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	6 (13.64%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Pain in extremity	5 (11.11%)	0 (0.00%)	3 (6.98%)	2 (4.65%)	1 (2.38%)	0 (0.00%)	3 (6.82%)	1 (2.27%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)										
Cancer pain	1 (2.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.27%)	1 (2.27%)	2 (9.52%)	0 (0.00%)
Tumour pain	2 (4.44%)	0 (0.00%)	1 (2.33%)	1 (2.33%)	1 (2.38%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	1 (4.76%)	0 (0.00%)
Nervous system disorders										
Dizziness	3 (6.67%)	0 (0.00%)	2 (4.65%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	1 (4.76%)	0 (0.00%)
Headache	3 (6.67%)	0 (0.00%)	5 (11.63%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	4 (9.09%)	0 (0.00%)	2 (9.52%)	0 (0.00%)

Paraesthesia	1 (2.22%)	0 (0.00%)	1 (2.33%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	3 (6.82%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Psychiatric disorders										
Insomnia	2 (4.44%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)	4 (9.09%)	0 (0.00%)	1 (4.76%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders										
Cough	3 (6.67%)	0 (0.00%)	8 (18.60%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	8 (18.18%)	1 (2.27%)	0 (0.00%)	0 (0.00%)
Dyspnoea	1 (2.22%)	0 (0.00%)	6 (13.95%)	0 (0.00%)	8 (19.05%)	0 (0.00%)	4 (9.09%)	1 (2.27%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders										
Eczema	0 (0.00%)	0 (0.00%)	1 (2.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pruritus	11 (24.44%)	0 (0.00%)	6 (13.95%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	8 (18.18%)	1 (2.27%)	3 (14.29%)	0 (0.00%)
Rash	4 (8.89%)	0 (0.00%)	8 (18.60%)	0 (0.00%)	3 (7.14%)	0 (0.00%)	4 (9.09%)	1 (2.27%)	0 (0.00%)	0 (0.00%)
Vitiligo	4 (8.89%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.76%)	0 (0.00%)	2 (4.55%)	0 (0.00%)	2 (9.52%)	0 (0.00%)
Vascular disorders										

Hyperte nsion	1 (2.2 2%)	0 (0.0 0%)		0 (0.00 %)	0 (0.00 %)		0 (0.0 0%)	0 (0.0 0%)		3 (6.8 2%)	0 (0.0 0%)		0 (0.0 0%)	0 (0.0 0%)

Other Relevant Findings

NA

Conclusion

This study evaluated PDR001 in combination with either LAG525, INC280, ACZ885, or LEE011 in subjects with previously treated stage IIIB/C/D or IV unresectable or metastatic melanoma. At final analysis, confirmed overall response rate (ORR) was 8.9% in the PDR001+LAG525 arm (Arm 1), 4.7% in the PDR001+ INC280 arm (Arm 2), 4.7% in the PDR001+ ACZ885 arm (Arm 3), and 6.8% in the PDR001+ LEE011 arm (Arm 4) in the randomized section of the study. At final analysis, confirmed ORR was 14.3% in the PDR001+LAG525 arm (Arm 1A) in the non-randomized section of the study.

The safety data are consistent with the known and well-characterized safety profile of PDR001, LAG525, INC280, ACZ885, and LEE011.

Date of Clinical Trial Report

20-Jul-2023