NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis

Generic Drug Name

LAG525 and spartalizumab (PDR001)

Trial Indication(s)

Triple-negative breast cancer

Protocol Number

CLAG525B2101

Protocol Title

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

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2 (LAG525) and Phase 3 (PDR001)

Study Start/End Dates

Study Start Date: July 2018 (Actual)
Primary Completion Date: February 2020 (Actual)
Study Completion Date: November 2021 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was an open-label, Phase II, randomized, multicenter study to assess the efficacy, safety, and pharmacokinetic characteristics of the following three combinations: LAG525 + spartalizumab (PDR001) (Arm 1), LAG525 + spartalizumab (PDR001) + carboplatin (Arm 2), and LAG525 + carboplatin (Arm 3) in participants with advanced triple-negative breast cancer (TNBC) which progressed after adjuvant or one prior line of systemic therapy for metastatic disease.

Participants were assigned to one of the three treatment arms in a ratio of 1:1:1. In protocol amendment 3 (released on 28-Mar-2019), enrollment to treatment Arm 1 (LAG525 + spartalizumab) was prematurely closed due to a higher discontinuation rate due to progressive disease and all subsequent enrolled patients were randomized to Arms 2 and 3 only, in a ratio of 1:1.

Study treatment continued until disease progression, unacceptable toxicity, pregnancy, investigator/participant decision, start of a new anti-neoplastic therapy, withdrawal of consent, lost to follow-up, death, or study was terminated by the sponsor. The investigator might decide to stop carboplatin after 6 cycles, even if the above criteria were not met. Participants who continued to derive clinical benefit from the treatment based on the investigator's evaluation following their completion of this trial might receive post-trial access (PTA) i.e. rollover protocol or a post-study drug supply (PSDS).

The end of study was defined as the earliest occurrence of one of the following: (1) all participants had died or (2) discontinued from the study, or (3) another clinical study became available that could continue to provide study treatment in this participant population and all ongoing participants were eligible to be transferred to that clinical study.

Centers

33 centers in 17 countries: Australia(3), Belgium(1), Singapore(1), Taiwan(3), Canada(2), Korea, Republic of(2), Lebanon(3), United States(2), Italy(1), Japan(4), Hungary(2), Spain(2), Thailand(1), Germany(3), Israel(1), France(1), Argentina(1)

Objectives:

The primary objective was:

- To assess the antitumor activity of the three treatment arms LAG525 + spartalizumab, LAG525 + spartalizumab + carboplatin and LAG525 + carboplatin, in participants with advanced 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.

The secondary objectives were:

- To assess the efficacy of the three treatment arms with respect to Duration of response (DOR), Time to response (TTR), Progression Free Survival (PFS) and Clinical benefit rate (CBR) per investigator's assessment according to RECIST v1.1
- To assess Overall Survival (OS) for each treatment arm
- To characterize the safety profile of each treatment arm
- To characterize the pharmacokinetics (PK) of LAG525, spartalizumab, and carboplatin in the three investigated combinations
- To assess immunogenicity of LAG525 and spartalizumab in the three investigated combinations

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

- LAG525 was a concentrate for solution for intravenous infusion, came in 100mg vials as a liquid formulation for infusion and was dosed at 400mg every 21 days. For all arms, LAG525 was infused first.
- Spartalizumab was a concentrate for solution for intravenous infusion, came in 100mg vials as a liquid formulation for infusion and was dosed at 300mg every 21 days. Spartalizumab was infused after LAG525.
- Carboplatin was a concentrate for solution for intravenous infusion, came in 100mg/mL and was dosed per area under the curve (AUC) 6 every 21 days. Carboplatin was infused once LAG525 and spartalizumab infusions were completed.

Statistical Methods

The primary efficacy variable was the ORR defined as the proportion of participants with best overall response (BOR) of complete response (CR) or partial response (PR) after at least 24 weeks of efficacy follow up, as per local review and according to RECIST 1.1. BOR was defined as the best response recorded from the randomization date until disease progression as per RECIST 1.1. If any new antineoplastic therapy was taken while on study, any subsequent assessments were excluded from the best overall response determination. Complete and partial responses were required to be confirmed by repeat assessments performed no less than 4 weeks after the criteria for response were first met. The 95% CIs were computed using two-sided exact binomial method.

DoR, TTR, CBR and PFS were analyzed as per the investigator assessments according to RECIST v1.1. DoR, CBR and PFS were calculated using the Kaplan-Meier method and TTR using descriptive statistics.

Safety endpoints were analysed using Safety Set.

The PK parameters were derived based on non-compartmental methods. Descriptive statistics were calculated by treatment for the PK Analysis Set (PAS) for all PK parameters.

Immunogenicity was descriptively characterized by tabulating anti-drug antibodies (ADA) prevalence at baseline and ADA incidence on-treatment.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Had advanced (loco-regionally recurrent not amenable to curative therapy or metastatic) breast cancer
- Had adequate bone marrow and organ function.
- Had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Had measurable disease, i.e., at least one measurable lesion as per RECIST 1.1 criteria (Tumor lesions previously irradiated or subjected to other loco-regional therapy was to be considered measurable if disease progression at the treated site after completion of therapy is clearly documented)
- Progressed after adjuvant or 1 prior systemic treatment in the metastatic setting. Patients with de novo metastatic disease were eligible if they received 1 prior line of therapy
- Had received prior systemic treatment that included taxane-based chemotherapy for adjuvant or metastatic disease

• Had a site of disease amenable to biopsy, and was willing to undergo a new tumor biopsy at screening and during therapy on this study, the latter if medically feasible. Patients with an available archival tumor tissue did not need to perform a tumor biopsy at screening if patient had not received anti-cancer therapy since the biopsy was taken.
• Had histologically and/or cytologically confirmed diagnosis of advanced TNBC (based on most recently analyzed biopsy from locally recurrent or metastatic site, local lab) meeting the following criteria: HER2 negative in situ hybridization test or an IHC status of 0 or 1+, and ER and PR expression was <1 percent as determined by immunohistochemistry (IHC)

Exclusion Criteria:
• Had received prior immune checkpoint inhibitors as anticancer treatment such as anti-LAG-3, anti-PD-1, anti-PD-L1, or anti-PD-L2 antibody (any line of therapy)
• Received prior neoadjuvant or adjuvant therapy with a platinum agent or mitomycin and experienced recurrence within 12 months after the end of the platinum-based or mitomycin containing therapy or received Platinum or mitomycin for metastatic disease
• Had major surgery within 14 days prior to starting study treatment or had not recovered to grade 1 or less from major side effects
• Presence of CTCAE grade 2 toxicity or higher due to prior cancer therapy. Exception to this criterion; patients with any grade of alopecia were allowed to enter the study.
• Had received radiotherapy ≤ 4 weeks prior to randomization (≤ 2 weeks for limited field radiation for palliation), and had not recovered to grade 1 or better from related side effects of such therapy (with the exception of alopecia)
• Had a known hypersensitivity to other monoclonal antibodies, platinum-containing compounds, or to any of the excipients of LAG525, spartalizumab, or carboplatin
• Had symptomatic central nervous system (CNS) metastases or CNS metastases that required local CNS-directed therapy (such as radiotherapy or surgery), or increasing doses of corticosteroids within the 2 weeks prior to first dose of study treatment. Patients with treated brain metastases would be neurologically stable and without CNS progression for at least 12 weeks prior to randomization and had discontinued corticosteroid treatment (with the exception of < 10 mg/day of prednisone or equivalent for an indication other than CNS metastases) for at least 4 weeks before first dose of any study treatment
• Had clinically significant cardiac disease or impaired cardiac function

Participant Flow Table

Overall Study

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	Total

Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	
Started	20	34	34	88
Treated	19	34	34	87
Completed	0	0	0	0
Not Completed	20	34	34	88
Adverse Event	2	3	3	8
Death	0	0	1	1
Physician Decision	3	6	6	15
Progressive disease	15	23	23	61
Patient decision	0	1	1	2
Terminated by sponsor (end of study definition was met)	0	1	0	1

Baseline Characteristics

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin	Total
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	
Number of Participants [units: participants]	20	34	34	88
Age Continuous (units: Years) Mean ± Standard Deviation				
	53.8±10.22	50.9±10.88	53.3±10.78	52.5±10.65
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)				
Female	20	34	34	88
Male	0	0	0	0
Race/Ethnicity, Customized (units: Participants) Count of Participants (Not Applicable)				
Asian	8	8	7	23
Black or African American	0	0	1	1
Missing	0	3	1	4
White	12	23	25	60

Primary Outcome Result(s)

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

(Time Frame: Up to approximately 14 months)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	20	34	34
Overall response rate (ORR) per investigator's assessment according to RECIST v1.1 (units: Percentage of participants) Number (95% Confidence Interval)			
	5.0 (0.1 to 24.9)	32.4 (17.4 to 50.5)	17.6 (6.8 to 34.5)

Secondary Outcome Result(s)

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

(Time Frame: Up to approximately 14 months)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	20	34	34
Clinical Benefit Rate (CBR) per investigator's assessment according to RECIST v1.1 (units: Percentage of Participants) Number (95% Confidence Interval)			
	5.0 (0.1 to 24.9)	35.3 (19.7 to 53.5)	20.6 (8.7 to 37.9)

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

(Time Frame: From first documented response up to disease progression or death due to underlying cancer, whichever occurs first, up to approximately 14 months)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin

Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	1	11	6
Duration of response (DOR) per investigator's assessment according to RECIST v1.1 (units: Months) Median (95% Confidence Interval)			
	4.9 (NA to NA)[1]	13.6 (2.8 to NA)[2]	12.6 (2.4 to NA)[3]

[1] NA: Confidence Interval was not estimable due to the low number of events
[2] NA: Upper limit of the confidence Intervals was not estimable due to the low number of events
[3] NA: Upper limit of the confidence Intervals was not estimable due to the low number of events

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

(Time Frame: From date of randomization to first documented response (CR or PR), up to approximately 14 months)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion	Participants received LAG525, PDR001 and carboplatin administered as infusion	Participants received LAG525 and carboplatin administered as infusion

	once every 3 weeks	once every 3 weeks.	once every 3 weeks
Number of Participants Analyzed [units: participants]	1	11	6
Time to response (TTR) per investigator's assessment according to RECIST v1.1 (units: Months) Median (Full Range)			
	1.5 (1.5 to 1.5)	1.7 (1.2 to 4.1)	1.4 (1.2 to 2.8)

Progression free survival (PFS)

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

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	20	34	34
Progression free survival (PFS) (units: Months) Median (95% Confidence Interval)			

1.4 (1.2 to 1.5)	4.3 (2.8 to 5.6)	3.0 (2.2 to 5.5)

Overall Survival (OS)

(Time Frame: From date of randomization to date of death due to any cause, up to 18 months)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	20	34	34
Overall Survival (OS) (units: Months) Median (95% Confidence Interval)			
	6.1 (4.6 to NA)[1]	11.6 (7.5 to NA)[2]	8.0 (6.2 to 9.3)

[1] NA: Upper limit of the confidence interval was not estimable due to the low number of events
[2] NA: Upper limit of the confidence interval was not estimable due to the low number of events

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

(Time Frame: 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)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	11	24	33
Pharmacokinetics (PK) parameter, Area under the plasma concentration versus time curve from time 0 to 504 hours (AUC0-504h) of LAG525 (units: day*microgram/miliLiter (day*ug/mL)) Geometric Mean (Geometric Coefficient of Variation)			
Cycle 1	1270 (25.8%)	1350 (22.4%)	1180 (23.4%)
Cycle 3	2060 (60.1%)	2200 (34.4%)	1990 (31.3%)

PK parameter, Cmax of LAG525

(Time Frame: 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)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion	Participants received LAG525, PDR001 and carboplatin administered as infusion	Participants received LAG525 and carboplatin administered as infusion

	once every 3 weeks	once every 3 weeks.	once every 3 weeks
Number of Participants Analyzed [units: participants]	16	34	30
PK parameter, Cmax of LAG525 (units: ug/mL) Geometric Mean (Geometric Coefficient of Variation)			
Cycle 1	127 (26.5%)	136 (21.1%)	128 (17.9%)
Cycle 3	144 (48.9%)	181 (29.5%)	168 (26.6%)

PK parameter, AUClast of LAG525

(Time Frame: 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)

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	16	34	29
PK parameter, AUClast of LAG525 (units: day*ug/mL) Geometric Mean (Geometric Coefficient of Variation)			
Cycle 1	1170 (32.0%)	1310 (41.1%)	1010 (151.2%)
Cycle 3	240 (9775.4%)	2040 (49.8%)	1490 (196.4%)

PK parameter, Tmax of LAG525

(Time Frame: 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)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	16	34	30
PK parameter, Tmax of LAG525 (units: hr) Geometric Mean (Geometric Coefficient of Variation)			
Cycle 1	1.51 (40.7%)	1.76 (35.5%)	1.58 (23.1%)
Cycle 3	1.64 (13.4%)	1.58 (15.0%)	1.77 (37.4%)

PK parameter, AUC0-504h of PDR001

(Time Frame: 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)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin
Arm/Group Description	Participants received LAG525 and PDR001	Participants received LAG525, PDR001 and

	administered as infusion once every 3 weeks	carboplatin administered as infusion once every 3 weeks.
Number of Participants Analyzed [units: participants]	11	24
PK parameter, AUC0-504h of PDR001 (units: day*ug/mL) Mean ± Standard Deviation		
Cycle 1	819 ± 23.6	907 ± 29.1
Cycle 3	1490 ± 41.0	1710 ± 29.5

PK parameter, Cmax of PDR001

(Time Frame: 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)

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.
Number of Participants Analyzed [units: participants]	16	33
PK parameter, Cmax of PDR001 (units: ug/mL) Geometric Mean (Geometric Coefficient of Variation)		

Cycle 1	78.0 (18.9%)	82.4 (25.1%)
Cycle 3	95.1 (41.4%)	117 (26.8%)

PK parameter, AUClast of PDR001

(Time Frame: 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)

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.
Number of Participants Analyzed [units: participants]	16	33
PK parameter, AUClast of PDR001 (units: day*ug/mL) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	780 (24.4%)	890 (44.6%)
Cycle 3	374 (2703.2%)	1500 (55.7%)

PK parameter, Tmax of PDR001

(Time Frame: 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)

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**

Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.
Number of Participants Analyzed [units: participants]	16	33
PK parameter, Tmax of PDR001 (units: hr) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	1.43 (34.7%)	1.71 (29.7%)
Cycle 3	1.67 (13.6%)	1.61 (13.9%)

PK parameter, AUC0-4h of carboplatin (total platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks

Number of Participants Analyzed [units: participants]	24	20
PK parameter, AUC0-4h of carboplatin (total platinum) (units: hour*nanogram/miliLiter (hr*ng/mL)) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	45000 (23.0%)	45200 (16.1%)
Cycle 3	42700 (27.6%)	43500 (29.2%)

PK parameter, Cmax of carboplatin (total platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	33	31
PK parameter, Cmax of carboplatin (total platinum) (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	22300 (32.0%)	21400 (32.2%)
Cycle 3	20900 (33.4%)	20000 (199.2%)

PK parameter, AUClast of carboplatin (total platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	33	29
PK parameter, AUClast of carboplatin (total platinum) (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	42000 (30.8%)	38900 (56.3%)
Cycle 3	40800 (38.1%)	42600 (43.3%)

PK parameter, Tmax of carboplatin (total platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin	Participants received LAG525 and carboplatin administered

	administered as infusion once every 3 weeks.	as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	33	31
PK parameter, Tmax of carboplatin (total platinum) (units: hr) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	0.857 (35.5%)	0.720 (31.9%)
Cycle 3	0.789 (33.0%)	0.720 (34.8%)

PK parameter, AUC0-4h of carboplatin (ultrafilterable platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	12	7
PK parameter, AUC0-4h of carboplatin (ultrafilterable platinum) (units: hour*nanogram/miliLiter (hr*ng/mL)) Geometric Mean (Geometric Coefficient of Variation)		

Cycle 1	43600 (13.1%)	44700 (23.4%)
Cycle 3	41100 (30.5%)	41000 (12.8%)

PK parameter, Cmax of carboplatin (ultrafilterable platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	15	19
PK parameter, Cmax of carboplatin (ultrafilterable platinum) (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	23200 (19.8%)	25700 (24.2%)
Cycle 3	22300 (40.1%)	14700 (4159.6%)

PK parameter, AUClast of carboplatin (ultrafilterable platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	**LAG525 + carboplatin**

Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	15	17
PK parameter, AUClast of carboplatin (ultrafilterable platinum) (units: ng/mL) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	41400 (13.0%)	35600 (65.2%)
Cycle 3	37400 (30.1%)	36300 (68.2%)

PK parameter, Tmax of carboplatin (ultrafilterable platinum)

(Time Frame: 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)

	LAG525+ PDR001+ carboplatin	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks

Number of Participants Analyzed [units: participants]	15	19
PK parameter, Tmax of carboplatin (ultrafilterable platinum) (units: hr) Geometric Mean (Geometric Coefficient of Variation)		
Cycle 1	0.802 (42.5%)	0.660 (34.4%)
Cycle 3	0.828 (39.7%)	0.686 (34.6%)

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

(Time Frame: Baseline)

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	18	34	33
Anti-drug antibodies (ADA) prevalence at baseline for LAG525 (units: Participants) Count of Participants (Not Applicable)			
	0 (%)	0 (%)	1 (3.03%)

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

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

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin	LAG525 + carboplatin
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	15	32	32
Anti-drug antibodies (ADA) incidence on treatment for LAG525 (units: Participants) Count of Participants (Not Applicable)			
	0 (%)	0 (%)	1 (3.13%)

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

(Time Frame: Baseline)

	LAG525 + PDR001	LAG525+ PDR001+ carboplatin
Arm/Group Description	Participants received LAG525 and	Participants received LAG525,

	PDR001 administered as infusion once every 3 weeks	PDR001 and carboplatin administered as infusion once every 3 weeks.
Number of Participants Analyzed [units: participants]	18	34
Anti-drug antibodies (ADA) prevalence at baseline for PDR001 (units: Participants) Count of Participants (Not Applicable)		
	3 (16.67%)	6 (17.65%)

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

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

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.
Number of Participants Analyzed [units: participants]	15	25

Anti-drug antibodies (ADA) incidence on treatment for PDR001 (units: Participants) Count of Participants (Not Applicable)		
	1 (6.67%)	0 (%)

Post-hoc: All collected deaths

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

	LAG525 + PDR001	**LAG525+ PDR001+ carboplatin**	**LAG525 + carboplatin**
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Number of Participants Analyzed [units: participants]	19	34	34
All collected deaths (units: Participants) Count of Participants (Not Applicable)			
On-treatment	0 (%)	2 (5.88%)	1 (2.94%)
Extended safety follow-up deaths	7 (36.84%)	7 (20.59%)	16 (47.06%)
Post-treatment deaths	8 (42.11%)	15 (44.12%)	11 (32.35%)

All deaths	15 (78.95%)	24 (70.59%)	28 (82.35%)

Safety Results

All-Cause Mortality

	LAG525 + PDR001 (On-treatment period) N = 19	LAG525 + PDR001 (Extended safety follow-up period) N = 19	LAG525 + PDR001+carboplatin (On-treatment period) N = 34	LAG525 + PDR001+carboplatin (Extended safety follow-up period) N = 34	LAG525 +carboplatin (On-treatment period) N = 34	LAG525 +carboplatin (Extended safety follow-up period) N = 34
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Total participants affected	0 (0.00%)	7 (36.84%)	2 (5.88%)	7 (20.59%)	1 (2.94%)	16 (47.06%)

Serious Adverse Events by System Organ Class

Time Frame	In the on-treatment period, adverse events (AEs) and serious AEs (including the All-Cause Mortality data table) are presented from first dose of study treatment until last dose of study treatment plus 30 days post treatment, up to 2.9 years In the extended safety follow-up period, AEs and serious AEs (including the All-Cause Mortality data table) are presented from day 31 to day 150 after last administration of study treatment, up to 3.2 years
Additional Description	The safety analysis was performed in the safety set including all participants who received at least one dose of study treatment (i.e., at least one dose of any component of the study treatment, including incomplete infusion of spartalizumab, LAG525 or carboplatin).

Source Vocabulary for Table Default	MedDRA (24.1)
Assessment Type for Table Default	Systematic Assessment

	LAG525 + PDR001 (On-treatment period) N = 19	LAG525 + PDR001 (Extended safety follow-up period) N = 19	LAG525 + PDR001+carboplatin (On-treatment period) N = 34	LAG525 + PDR001+carboplatin (Extended safety follow-up period) N = 34	LAG525 +carboplatin (On-treatment period) N = 34	LAG525 +carboplatin (Extended safety follow-up period) N = 34
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Total participants affected	6 (31.58%)	0 (0.00%)	12 (35.29%)	6 (17.65%)	14 (41.18%)	2 (5.88%)
Blood and lymphatic system disorders						
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	1 (2.94%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders						
Atrial thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Myocardial infarction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Myocarditis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	0 (0.00%)
Pericardial effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)

Wolff-Parkinson-White syndrome	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Congenital, familial and genetic disorders						
Fanconi syndrome	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders						
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Erosive duodenitis	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Faeces discoloured	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Intestinal ischaemia	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
General disorders and administration site conditions						
Disease progression	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
General physical health deterioration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Malaise	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Hepatobiliary disorders						
Biliary colic	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations						
Pneumocystis jirovecii pneumonia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	0 (0.00%)
Septic shock	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Subcutaneous abscess	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications						
Thoracic vertebral fracture	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations						
Platelet count decreased	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Troponin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Metabolism and nutrition disorders						
Hypercalcaemia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders						
Back pain	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Metastases to meninges	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Nervous system disorders						
Brain oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)

Psychiatric disorders						
Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Renal and urinary disorders						
Renal tubular acidosis	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders						
Dyspnoea	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	3 (8.82%)	1 (2.94%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Interstitial lung disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Pleuritic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	In the on-treatment period, adverse events (AEs) and serious AEs (including the All-Cause Mortality data table) are presented from first dose of study treatment until last dose of study treatment plus 30 days post treatment, up to 2.9 years In the extended safety follow-up period, AEs and serious AEs (including the All-Cause Mortality data table) are presented from day 31 to day 150 after last administration of study treatment, up to 3.2 years
Additional Description	The safety analysis was performed in the safety set including all participants who received at least one dose of study treatment (i.e., at least one dose of any component of the study treatment, including incomplete infusion of spartalizumab, LAG525 or carboplatin).
Source Vocabulary for Table Default	MedDRA (24.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	LAG525 + PDR001 (On-treatment period) N = 19	LAG525 + PDR001 (Extended safety follow-up period) N = 19	LAG525 + PDR001+carboplatin (On-treatment period) N = 34	LAG525 + PDR001+carboplatin (Extended safety follow-up period) N = 34	LAG525 +carboplatin (On-treatment period) N = 34	LAG525 +carboplatin (Extended safety follow-up period) N = 34
Arm/Group Description	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525 and PDR001 administered as infusion once every 3 weeks	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525, PDR001 and carboplatin administered as infusion once every 3 weeks.	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks	Participants received LAG525 and carboplatin administered as infusion once every 3 weeks
Total participants affected	17 (89.47%)	0 (0.00%)	34 (100.00%)	11 (32.35%)	33 (97.06%)	3 (8.82%)
Blood and lymphatic system disorders						
Anaemia	1 (5.26%)	0 (0.00%)	20 (58.82%)	5 (14.71%)	19 (55.88%)	1 (2.94%)
Leukopenia	0 (0.00%)	0 (0.00%)	3 (8.82%)	0 (0.00%)	5 (14.71%)	0 (0.00%)
Neutropenia	0 (0.00%)	0 (0.00%)	9 (26.47%)	1 (2.94%)	7 (20.59%)	0 (0.00%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	15 (44.12%)	0 (0.00%)	14 (41.18%)	1 (2.94%)
Endocrine disorders						
Goitre	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypothyroidism	0 (0.00%)	0 (0.00%)	5 (14.71%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Thyroiditis	1 (5.26%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Eye disorders						
Dry eye	1 (5.26%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders						

Abdominal distension	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain	1 (5.26%)	0 (0.00%)	5 (14.71%)	2 (5.88%)	2 (5.88%)	0 (0.00%)
Abdominal pain upper	1 (5.26%)	0 (0.00%)	5 (14.71%)	0 (0.00%)	3 (8.82%)	0 (0.00%)
Constipation	3 (15.79%)	0 (0.00%)	7 (20.59%)	1 (2.94%)	16 (47.06%)	0 (0.00%)
Diarrhoea	0 (0.00%)	0 (0.00%)	5 (14.71%)	2 (5.88%)	7 (20.59%)	0 (0.00%)
Dry mouth	0 (0.00%)	0 (0.00%)	5 (14.71%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspepsia	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	3 (8.82%)	0 (0.00%)
Dysphagia	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	3 (8.82%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Nausea	3 (15.79%)	0 (0.00%)	18 (52.94%)	2 (5.88%)	13 (38.24%)	1 (2.94%)
Toothache	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	7 (20.59%)	1 (2.94%)	7 (20.59%)	0 (0.00%)
General disorders and administration site conditions						
Asthenia	0 (0.00%)	0 (0.00%)	11 (32.35%)	0 (0.00%)	5 (14.71%)	0 (0.00%)
Chest pain	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Chills	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	2 (10.53%)	0 (0.00%)	11 (32.35%)	1 (2.94%)	12 (35.29%)	0 (0.00%)
Gait disturbance	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Induration	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Influenza like illness	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Malaise	1 (5.26%)	0 (0.00%)	3 (8.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	2 (5.88%)	0 (0.00%)
Pain	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)

Pyrexia	1 (5.26%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	3 (8.82%)	1 (2.94%)
Infections and infestations						
Conjunctivitis	1 (5.26%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	1 (5.26%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	1 (2.94%)	0 (0.00%)
Lymphangitis	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	2 (5.88%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Rhinitis	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	2 (5.88%)	1 (2.94%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Urinary tract infection	1 (5.26%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	2 (5.88%)	0 (0.00%)
Injury, poisoning and procedural complications						
Contusion	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations						
Alanine aminotransferase increased	1 (5.26%)	0 (0.00%)	6 (17.65%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Aspartate aminotransferase increased	2 (10.53%)	0 (0.00%)	4 (11.76%)	1 (2.94%)	2 (5.88%)	0 (0.00%)
Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Blood creatine phosphokinase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)

Blood thyroid stimulating hormone increased	1 (5.26%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Gamma-glutamyltransferase increased	1 (5.26%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	11 (32.35%)	2 (5.88%)	6 (17.65%)	0 (0.00%)
Platelet count decreased	1 (5.26%)	0 (0.00%)	14 (41.18%)	2 (5.88%)	9 (26.47%)	0 (0.00%)
SARS-CoV-2 test negative	0 (0.00%)	0 (0.00%)	2 (5.88%)	1 (2.94%)	1 (2.94%)	0 (0.00%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (8.82%)	2 (5.88%)	0 (0.00%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	5 (14.71%)	1 (2.94%)	1 (2.94%)	0 (0.00%)
Metabolism and nutrition disorders						
Decreased appetite	2 (10.53%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	4 (11.76%)	0 (0.00%)
Hyperglycaemia	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypocalcaemia	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	0 (0.00%)	0 (0.00%)	4 (11.76%)	2 (5.88%)	2 (5.88%)	0 (0.00%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	4 (11.76%)	1 (2.94%)	3 (8.82%)	0 (0.00%)
Hyponatraemia	1 (5.26%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Hypophagia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Musculoskeletal and connective tissue disorders						
Arthralgia	1 (5.26%)	0 (0.00%)	3 (8.82%)	1 (2.94%)	4 (11.76%)	0 (0.00%)
Back pain	1 (5.26%)	0 (0.00%)	7 (20.59%)	2 (5.88%)	3 (8.82%)	0 (0.00%)
Bone pain	1 (5.26%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	1 (2.94%)	0 (0.00%)

Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	2 (5.88%)	2 (5.88%)	1 (2.94%)	0 (0.00%)
Musculoskeletal pain	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	2 (10.53%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neck pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	5 (14.71%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Metastases to skin	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders						
Dizziness	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	6 (17.65%)	0 (0.00%)
Dysgeusia	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Headache	2 (10.53%)	0 (0.00%)	8 (23.53%)	0 (0.00%)	4 (11.76%)	1 (2.94%)
Intercostal neuralgia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paraesthesia	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (2.94%)
Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	3 (8.82%)	0 (0.00%)
Somnolence	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders						
Anxiety	1 (5.26%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Insomnia	0 (0.00%)	0 (0.00%)	1 (2.94%)	1 (2.94%)	6 (17.65%)	0 (0.00%)
Renal and urinary disorders						
Polyuria	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Reproductive system and breast disorders						
Breast pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)
Pelvic pain	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vaginal discharge	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders						
Cough	2 (10.53%)	0 (0.00%)	7 (20.59%)	0 (0.00%)	4 (11.76%)	0 (0.00%)
Dyspnoea	1 (5.26%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	6 (17.65%)	0 (0.00%)
Haemoptysis	0 (0.00%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	1 (2.94%)	0 (0.00%)	3 (8.82%)	0 (0.00%)
Skin and subcutaneous tissue disorders						
Alopecia	0 (0.00%)	0 (0.00%)	3 (8.82%)	0 (0.00%)	3 (8.82%)	0 (0.00%)
Dry skin	3 (15.79%)	0 (0.00%)	3 (8.82%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eczema	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pruritus	2 (10.53%)	0 (0.00%)	4 (11.76%)	0 (0.00%)	1 (2.94%)	0 (0.00%)
Rash	2 (10.53%)	0 (0.00%)	6 (17.65%)	1 (2.94%)	1 (2.94%)	0 (0.00%)
Skin lesion	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders						
Hot flush	1 (5.26%)	0 (0.00%)	2 (5.88%)	0 (0.00%)	1 (2.94%)	0 (0.00%)

Other Relevant Findings

None

Conclusion:

The CLAG525B2101 study did not meet its primary objective for confirmed ORR (investigator assessment, RECIST 1.1) in any of the 3 treatment arms.

Overall, a higher ORR was observed for patients treated in the triplet arm (LAG525 + PDR001 + carboplatin) compared to the other two treatment arms, for patients treated in the first-line metastatic setting, and for patients without liver metastases at study entry.

The safety profile of the three treatment combinations has been well characterized in the intended target patient population and is consistent with the results from previous studies where these agents were used individually or in combination. It was consistent with the known and expected side effect profile of checkpoint inhibitors and the myelotoxic effects of carboplatin.

Considering the efficacy results of this study together with an increasingly crowded treatment landscape in metastatic TNBC, Novartis decided not to pursue LAG525 development in breast cancer.

Date of Clinical Trial Report

Primary Clinical Trial Report: 17-Dec-2020; Final Clinical Trial Report: 30-May-2022