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Sponsor

Novartis

Generic Drug Name

Spartalizumab (PDR001), LAG525, NIR178, capmatinib (INC280), MCS110 and canakinumab (ACZ885)

Trial Indication(s)

Triple negative breast cancer

Protocol Number

CADPT01A12101C

Protocol Title

A Phase Ib, multicenter, open-label dose escalation and expansion platform study of select immunotherapy combinations in adult patients with triple-negative breast cancer

Clinical Trial Phase

Phase 1

Phase of Drug Development

Spartalizumab (Phase 3), LAG525 (phase 2), NIR178 (phase 2), capmatinib (phase 4), MCS110 (phase 2) and canakinumab (phase 4)

Study Start/End Dates

Study Start Date: January 31, 2019 (Actual)
Primary Completion Date: February 06, 2023 (Actual)
Study Completion Date: February 06, 2023 (Actual)

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Reason for Termination (If applicable)

Novartis communicated to study investigators the decision to halt recruitment in the CADPT01A12101C study in the LAG525 + spartalizumab + MCS110 investigational arm (Arm 3) on 16 April 2020 due to discontinuation of the development program for MCS110, and in the LAG525 + spartalizumab + capmatinib investigational arm (Arm 2) on 20 July 2020 due to limited anti-tumor activity observed in this treatment arm. Ongoing patients at the time of enrolment halt of the two arms continued receiving study treatment as per protocol.

The recruitment halt of the CADPT01A12101C study was not a consequence of any safety concern and had no impact on any other clinical trials involving spartalizumab, LAG525, NIR178, capmatinib, MCS110 or canakinumab.

Study Design/Methodology

This was a Phase Ib, multi-center, open-label dose-escalation study with multiple treatment arms. The study design consisted of a dose-escalation and a dose-expansion part.

Investigational drugs were considered either “backbone” or “partner.” The combination of a backbone (spartalizumab + LAG525) and a partner (NIR178, capmatinib, MCS110 or canakinumab) constituted a treatment arm.

During the dose-escalation part of each treatment arm, subjects were treated with fixed doses of backbone study drugs in combination with variable doses of the partner investigational drug. Multiple triplet combination treatment arms were enrolled in parallel during dose escalation:

Arm 1: Spartalizumab + LAG525 in combination with NIR178

Arm 2: Spartalizumab + LAG525 in combination with capmatinib

Arm 3: Spartalizumab + LAG525 in combination with MCS110

Arm 4: Spartalizumab + LAG525 in combination with canakinumab

Dose escalation and determination of the maximum tolerated dose (MTD)/recommended dose for expansion (RDE) was guided by a Bayesian logistic regression model (BLRM) with escalation with overdose control (EWOC) criteria.

The treatment arms for which an MTD/RDE could be reached and were determined to be safe could proceed to dose expansion to further explore safety, tolerability, and anti-tumor activity. However, there was no requirement to proceed to dose expansion once MTD/RDE was established during the dose-escalation phase of a treatment arm.

After the determination of the MTD/RDE for Arm 1 and Arm 4, dose expansion was not opened as per protocol. Thus, none of the four arms opened up for the expansion part.

Centers

13 centers in 9 countries/regions: Israel(1), Japan(1), Italy(2), Spain(2), Australia(1), Hong Kong(1), United States(2), Netherlands(1), Singapore(2)

Objectives:

The primary objective of the trial was to characterize the safety and tolerability of each treatment arm tested and identify recommended doses and regimens for future studies.

The secondary objectives of the trial were:

- To characterize the pharmacokinetic profile of each investigational drug within each treatment arm
- To assess immunogenicity of monoclonal antibodies
- To evaluate preliminary antitumor activity of each treatment arm
- To assess the pharmacodynamics effect of each treatment arm

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

For this study, the term "investigational drug" or "study drug" refers to spartalizumab (PDR001), LAG525, NIR178, capmatinib (INC280), MCS110 or canakinumab (ACZ885). "Study treatment" refers to a specific combination treatment.

The doses for backbone agents, spartalizumab and LAG525 were fixed at 400 mg every 28 days (Q4W) and 600 mg Q4W, respectively, for all treatment arms. Both study drugs were administered by intravenous (i.v.) infusion.

NIR178 (80, 160 and 240 mg) was administered orally as capsules twice daily (BID).

Capmatinib (200 and 300 mg) was administered orally as tablets BID.

MCS110 5 mg/kg was administered by i.v. infusion Q4W.

Canakinumab 600 mg was administered by subcutaneous injection every 56 days (Q8W).

A cycle of treatment was defined as 28 days.

A subject continued study treatment until the subject experienced unacceptable toxicity, disease progression per iRECIST and/or treatment was discontinued at the discretion of the investigator or the subject.

Statistical Methods

The analysis of the data was based on the following analysis sets:

The Full Analysis Set (FAS) comprised all subjects that received any study drug. Subjects were analyzed according to the study treatment received which was defined as the treatment most frequently taken between Study Day 1 and either the end of cycle 1, the onset of a dose-limiting toxicity (DLT), or treatment discontinuation, whichever occurred first.

The Safety Set was defined similarly as the FAS.

The Dose-Determining Set (DDS) included all subjects from the FAS (escalation part) who met the minimum exposure criterion and had sufficient safety evaluations or had experienced a DLT during cycle 1.

Minimum exposure criterion was defined as:

- For subject receiving LAG525+ spartalizumab+NIR178 (Arm 1), the subject received the planned doses for LAG525 and spartalizumab during the first cycle and took at least 75% of the planned doses for NIR178 during the first cycle.
- For subject receiving LAG525+ spartalizumab+capmatinib (Arm 2), the subject received the planned doses for LAG525 and spartalizumab during the first cycle and took at least 75% of the planned doses for capmatinib during the first cycle.

- For subject receiving LAG525+ spartalizumab+MCS110 (Arm 3), the subject received all the planned doses for LAG525, spartalizumab and MCS110 during the first cycle.
- For subject receiving LAG525+ spartalizumab+canakinumab (Arm 4), the subject received all the planned doses for LAG525, spartalizumab and canakinumab during the first cycle.

Subjects who did not experience a DLT during cycle 1 were considered to have sufficient safety evaluations if they were observed for more than 1 cycle and were considered by both the sponsor and investigators to have enough safety data to conclude that a DLT did not occur. Subjects were analyzed according to the study treatment received as defined for FAS.

The Pharmacokinetic analysis set (PAS) included all subjects who provided an evaluable pharmacokinetics (PK) profile. A profile was considered evaluable if all the following conditions were satisfied:

- Subject received one of the planned treatments
- Subject provided at least one primary PK parameter

The Immunogenicity (IG) prevalence set included all subjects in the Safety set with a non-missing baseline anti-drug antibody (ADA) sample or at least one non-missing post-baseline ADA sample.

The Immunogenicity incidence set included all subjects in the Immunogenicity prevalence set with a non-missing baseline ADA sample and at least one non-missing post-baseline ADA sample.

Study Population: Key Inclusion/Exclusion Criteria

Main Inclusion Criteria:

- Patients with advanced/metastatic TNBC (defined as HER-2 negative with <1% of tumor cell nuclei immunoreactive for estrogen receptor (ER) and progesterone receptor (PR)), with measurable disease as determined by RECIST version 1.1 (refer to Appendix 16.1). Tumor lesions previously irradiated or subjected to other loco-regional therapy will only be considered measurable if there is documented disease progression at the treated site prior to study entry.

- Patients should have received standard chemotherapy for advanced or metastatic disease but should not have received more than 2 prior lines of chemotherapy. Neoadjuvant or adjuvant chemotherapy will count as one prior line.
- Patients must have received prior systemic treatment that included taxane-based chemotherapy for neoadjuvant or metastatic disease.
- Patients must have a site of disease amenable to core needle biopsy, and be a candidate for tumor biopsy according to the treating institution's guidelines. Patients must be willing to undergo a new tumor biopsy at screening, and during therapy on the study. Exceptions may be considered after documented discussion with Novartis. Patients with available archival tumor tissue obtained ≤6 months prior to study treatment initiation do not need to undergo a new tumor biopsy at screening, if the patient has not received any anti-cancer therapy since the biopsy was taken, and if adequate tissue is available.

Main exclusion criteria applicable to all treatment arms:

- Patient has received prior treatment with anti-LAG-3, anti-PD-1, anti-PD-L1, or anti-PD-L2 antibody (any line of therapy).
- Presence of symptomatic central nervous system (CNS) metastases, or CNS metastases that require local CNS-directed therapy (such as radiotherapy or surgery), or increasing doses of corticosteroids within 2 weeks prior to initiating study treatment.
- History of severe hypersensitivity reactions to any ingredient of study drug(s) and other mAbs and/or their excipients.
- Impaired cardiac function or clinically significant cardiac disease.
- HIV infection.
- Patients with active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, including those with inactive disease for patients receiving either capmatinib, MCS110 or canakinumab.
- Active, known or suspected autoimmune disease.
- History of or current interstitial lung disease or pneumonitis grade ≥ 2.
- Subjects with tuberculosis (TB), for patients receiving either MCS110 or canakinumab.

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Participant Flow Table

Overall Study

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W	Total
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)	
Started	7	12	5	8	5	10	17	64
Completed	0	0	0	0	0	0	0	0
Not Completed*	7	12	5	8	5	10	17	64
Adverse Event	1	0	1	2	0	0	2	6
Physician Decision	1	2	0	0	1	2	3	9
Progressive Disease	5	9	4	6	4	8	12	48
Subject Decision	0	1	0	0	0	0	0	1

*Treatment discontinued

Baseline Characteristics

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W	Total
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)	
Number of Participants [units: participants]	7	12	5	8	5	10	17	64
Baseline Analysis Population Description								
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation								
	62.4±8.46	56.6±12.46	52.0±7.65	49.4±8.37	52.2±17.34	43.3±10.47	51.8±11.54	52.3±11.67
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								
Female	7	12	5	8	5	10	17	64

Male	0	0	0	0	0	0	0	0
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)								
Asian	1	3	2	0	2	1	8	17
White	6	9	3	8	3	9	9	47

Primary Outcome Result(s)

Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period

Description	Number of participants with AEs (any AE regardless of seriousness) and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. The on-treatment period is defined from the day of first administration of study treatment up to 30 days after the date of its last administration.
Time Frame	From first dose of study treatment to 30 days after last dose, up to 3.5 years (Arm 1), 0.5 years (Arm 2), 3.3 years (Arm 3) and 2.8 years (Arm 4)
Analysis Population Description	All patients who received any study drug

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab +	Arm 1: spartalizumab +	Arm 1: spartalizumab +	Arm 2: spartalizumab +	Arm 2: spartalizumab +	Arm 3: spartalizumab +	Arm 4: spartalizumab +

	LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
AEs	7 (100%)	12 (100%)	5 (100%)	8 (100%)	5 (100%)	10 (100%)	17 (100%)
Treatment-related AEs	6 (85.71%)	11 (91.67%)	4 (80%)	8 (100%)	5 (100%)	9 (90%)	11 (64.71%)
SAEs	2 (28.57%)	6 (50%)	2 (40%)	4 (50%)	4 (80%)	4 (40%)	10 (58.82%)
Treatment-related SAEs	2 (28.57%)	4 (33.33%)	1 (20%)	3 (37.5%)	2 (40%)	0 (%)	5 (29.41%)

Number of participants with Dose-Limiting Toxicities (DLTs) in the dose escalation part

Description	A dose-limiting toxicity (DLT) is defined as an adverse event or abnormal laboratory value of Common Terminology Criteria for Adverse Events (CTCAE) grade ≥ 3 assessed as unrelated to disease, disease progression, inter-current illness or concomitant medications that occurs within the first cycle of treatment during the dose escalation part of the study. Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher. The duration of one treatment cycle is 28 days.
Time Frame	28 days
Analysis Population Description	Patients who received any study drug and who either met the minimum exposure criterion defined in the protocol and had sufficient safety evaluations, or had experienced a DLT during cycle 1.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	10	3	7	3	9	15
Number of participants with Dose-Limiting Toxicities (DLTs) in the dose escalation part (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
	0 (%)	2 (20%)	2 (66.67%)	2 (28.57%)	2 (66.67%)	0 (%)	0 (%)

Number of participants with dose reductions or interruptions of spartalizumab

Description: Number of participants with at least one dose reduction or interruption of spartalizumab. For participants who did not tolerate the protocol-specified dosing schedule, dose adjustments were permitted in order to allow the participant to continue the study treatment. Dose reductions were not permitted for spartalizumab.

Time Frame: From first dose of study treatment to last dose, up to 3.4 years (Arm 1), 0.4 years (Arm 2), 3.2 years (Arm 3) and 2.7 years (Arm 4).

Analysis Population Description: All patients who received at least one dose of spartalizumab

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Number of participants with dose reductions or interruptions of spartalizumab (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
	3 (42.86%)	2 (16.67%)	1 (20%)	0 (%)	0 (%)	2 (20%)	6 (35.29%)

Number of participants with dose reductions or interruptions of LAG525

Description: Number of participants with at least one dose reduction or interruption of LAG525. For participants who did not tolerate the protocol-specified dosing schedule, dose adjustments were permitted in order to allow the participant to continue the study treatment. Dose reductions were not permitted for LAG525.

Time Frame	From first dose of study treatment to last dose, up to 3.4 years (Arm 1), 0.4 years (Arm 2), 3.2 years (Arm 3) and 2.7 years (Arm 4)
Analysis Population Description	All patients who received at least one dose of LAG525

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Number of participants with dose reductions or interruptions of LAG525 (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
	2 (28.57%)	2 (16.67%)	1 (20%)	0 (%)	0 (%)	2 (20%)	6 (35.29%)

Number of participants with dose reductions or interruptions of NIR178

Description	Number of participants with at least one dose reduction or interruption of NIR178. For participants who did not tolerate the protocol-specified dosing schedule, dose adjustments were permitted in order to allow the participant to continue the study treatment.
Time Frame	From first dose of study treatment to last dose, up to 3.4 years (Arm 1)

Analysis Population Description	All patients who received at least one dose of NIR178

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)
Number of Participants Analyzed [units: participants]	7	12	5
Number of participants with dose reductions or interruptions of NIR178 (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
	4 (57.14%)	3 (25%)	1 (20%)

Number of participants with dose reductions or interruptions of capmatinib

Description	Number of participants with at least one dose reduction or interruption of capmatinib. For participants who did not tolerate the protocol-specified dosing schedule, dose adjustments were permitted in order to allow the participant to continue the study treatment.
Time Frame	From first dose of study treatment to last dose, up to 0.4 years (Arm 2)
Analysis Population Description	All patients who received at least one dose of capmatinib

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID
Arm/Group Description	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)

Number of Participants Analyzed [units: participants]	8	5
Number of participants with dose reductions or interruptions of capmatinib (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
	1 (12.5%)	3 (60%)

Number of participants with dose reductions or interruptions of MCS110

Description	Number of participants with at least one dose reduction or interruption of MCS110. For participants who did not tolerate the protocol-specified dosing schedule, dose adjustments were permitted in order to allow the participant to continue the study treatment.
Time Frame	From first dose of study treatment to last dose, up to 3.2 years (Arm 3)
Analysis Population Description	All patients who received at least one dose of MCS110

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W
Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)
Number of Participants Analyzed [units: participants]	10
Number of participants with dose reductions or interruptions of MCS110 (units: participants)	**Count of Participants (Percentage)**
	2 (20%)

Number of participants with dose reductions or interruptions of canakinumab

Description	Number of participants with at least one dose reduction or interruption of canakinumab. For participants who did not tolerate the protocol-specified dosing schedule, dose adjustments were permitted in order to allow the participant to continue the study treatment.
Time Frame	From first dose of study treatment to last dose, up to 2.7 years (Arm 4)

Analysis Population Description	All patients who received at least one dose of canakinumab

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	17
Number of participants with dose reductions or interruptions of canakinumab (units: participants)	**Count of Participants (Percentage)**
	4 (23.53%)

Dose intensity of spartalizumab

Description	Dose intensity of spartalizumab was calculated as actual cumulative dose in milligrams divided by duration of exposure in days and then multiplied by 28 days.
Time Frame	From first dose of study treatment to last dose, up to 3.4 years (Arm 1), 0.4 years (Arm 2), 3.2 years (Arm 3) and 2.7 years (Arm 4)
Analysis Population Description	All patients who received at least one dose of spartalizumab

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in	Arm 1: spartalizumab + LAG525 (backbone) in	Arm 1: spartalizumab + LAG525 (backbone) in	Arm 2: spartalizumab + LAG525 (backbone) in	Arm 2: spartalizumab + LAG525 (backbone) in	Arm 3: spartalizumab + LAG525 (backbone) in	Arm 4: spartalizumab + LAG525 (backbone) in

	combination with NIR178 80 mg BID (partner)	combination with NIR178 160 mg BID (partner)	combination with NIR178 240 mg BID (partner)	combination with capmatinib 200 mg BID (partner)	combination with capmatinib 300 mg BID (partner)	combination with MCS110 5 mg/kg Q4W (partner)	combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Dose intensity of spartalizumab (units: mg/28 days)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	393.1 (317.7 to 400.0)	400.0 (268.3 to 407.3)	400.0 (343.3 to 589.5)	400.0 (400.0 to 407.3)	400.0 (386.2 to 448.0)	400.0 (347.3 to 402.9)	400.0 (275.4 to 466.7)

Dose intensity of LAG525

Description	Dose intensity of LAG525 was calculated as actual cumulative dose in milligrams divided by duration of exposure in days and then multiplied by 28 days.
Time Frame	From first dose of study treatment to last dose, up to 3.4 years (Arm 1), 0.4 years (Arm 2), 3.2 years (Arm 3) and 2.7 years (Arm 4).
Analysis Population Description	All patients who received at least one dose of LAG525

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5	Arm 4: spartalizumab + LAG525 (backbone) in combination with

	mg BID (partner)	160 mg BID (partner)	240 mg BID (partner)	200 mg BID (partner)	300 mg BID (partner)	mg/kg Q4W (partner)	canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Dose intensity of LAG525 (units: mg/28 days)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	600.0 (487.0 to 600.0)	600.0 (301.8 to 610.9)	600.0 (514.9 to 884.2)	600.0 (600.0 to 610.9)	600.0 (579.3 to 672.0)	600.0 (535.4 to 604.3)	600.0 (413.1 to 700.0)

Dose intensity of NIR178

Description	Dose intensity of NIR178 was calculated as actual cumulative dose in milligrams divided by duration of exposure in days.
Time Frame	From first dose of study treatment to last dose, up to 3.4 years (Arm 1)
Analysis Population Description	All patients who received at least one dose of NIR178

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)
Number of Participants Analyzed [units: participants]	7	12	5
Dose intensity of NIR178 (units: mg/day)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	156.2 (38.5 to 160.0)	320.0 (160.0 to 320.0)	475.7 (400.0 to 480.0)

Dose intensity of capmatinib

Description	Dose intensity of capmatinib was calculated as actual cumulative dose in milligrams divided by duration of exposure in days.
Time Frame	From first dose of study treatment to last dose, up to 0.4 years (Arm 2)
Analysis Population Description	All patients who received at least one dose of capmatinib

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**
Arm/Group Description	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)
Number of Participants Analyzed [units: participants]	8	5
Dose intensity of capmatinib (units: mg/day)	**Median (Full Range)**	**Median (Full Range)**
	400.0 (354.0 to 400.0)	575.7 (330.0 to 600.0)

Dose intensity of MCS110

Description	Dose intensity of MCS110 was calculated as actual cumulative dose in mg/kg divided by duration of exposure in days and then multiplied by 28 days.
Time Frame	From first dose of study treatment to last dose, up to 3.2 years (Arm 3)
Analysis Population Description	All patients who received at least one dose of MCS110

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W

Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)
Number of Participants Analyzed [units: participants]	10
Dose intensity of MCS110 (units: mg/kg/28 days)	**Median** **(Full Range)**
	5.0 (3.6 to 5.0)

Dose intensity of canakinumab

Description	Dose intensity of canakinumab was calculated as actual cumulative dose in milligrams divided by duration of exposure in days and then multiplied by 28 days.
Time Frame	From first dose of study treatment to last dose, up to 2.7 years (Arm 4)
Analysis Population Description	All patients who received at least one dose of canakinumab

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	17
Dose intensity of canakinumab (units: mg/28 days)	**Median** **(Full Range)**
	300.0 (259.8 to 700.0)

NOVARTIS

Secondary Outcome Result(s)

Maximum observed serum concentration (Cmax) of PDR001

Description	Pharmacokinetic (PK) parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the PDR001 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received PDR001 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	8	3	6	4	8	15
Maximum observed serum concentration (Cmax) of PDR001 (units: µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**

Cycle 1 Day 1 (n=7,8,3,6,4,8,15)	100 (35.9%)	117 (22.4%)	104 (12.5%)	106 (20.9%)	127 (34.7%)	139 (15.0%)	122 (35.3%)
Cycle 3 Day 1 (n=3,1,1,2,0,3,5)	180 (12.8%)	122	219	90.8 (4.5%)		164 (7.7%)	169 (26.0%)

Time to reach maximum serum concentration (Tmax) of PDR001

Description	PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the PDR001 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received PDR001 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	8	3	6	4	8	15
Time to reach maximum serum concentration	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**

(Tmax) of PDR001 (units: hours)							
Cycle 1 Day 1 (n=7,8,3,6,4,8,15)	0.533 (0.5 to 1.42)	0.667 (0.5 to 1.77)	0.85 (0.6 to 0.967)	0.533 (0.5 to 0.7)	0.567 (0.5 to 0.75)	0.567 (0.5 to 0.667)	0.6 (0.5 to 0.833)
Cycle 3 Day 1 (n=3,1,1,2,0,3,5)	0.667 (0.5 to 1.17)	0.5 (0.5 to 0.5)	0.867 (0.867 to 0.867)	0.542 (0.5 to 0.583)		0.5 (0.5 to 0.667)	0.667 (0.533 to 1.07)

Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of PDR001

Description	PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the PDR001 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received PDR001 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)

Number of Participants Analyzed [units: participants]	7	12	3	8	4	9	15
Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of PDR001 (units: hr*µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=7,12,3,8,4,9,15)	30700 (57.4%)	29200 (41.2%)	22700 (17.9%)	26700 (23.2%)	34100 (27.8%)	34600 (32.1%)	35100 (23.6%)
Cycle 3 Day 1 (n=3,2,1,2,0,3,6)	68900 (14.4%)	35100 (54.6%)	46000	27100 (44.8%)		61500 (29.0%)	52100 (57.1%)

Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of PDR001

Description	PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC0-672 calculation.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the PDR001 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received PDR001 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in	Arm 1: spartalizumab + LAG525 (backbone) in	Arm 1: spartalizumab + LAG525 (backbone) in	Arm 2: spartalizumab + LAG525 (backbone) in	Arm 2: spartalizumab + LAG525 (backbone) in	Arm 3: spartalizumab + LAG525 (backbone) in	Arm 4: spartalizumab + LAG525 (backbone) in

	combination with NIR178 80 mg BID (partner)	combination with NIR178 160 mg BID (partner)	combination with NIR178 240 mg BID (partner)	combination with capmatinib 200 mg BID (partner)	combination with capmatinib 300 mg BID (partner)	combination with MCS110 5 mg/kg Q4W (partner)	combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	6	8	2	2	2	6	14
Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of PDR001 (units: hr*µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=6,8,2,2,2,6,14)	34300 (34.5%)	31500 (33.8%)	22100 (24.5%)	33400 (12.8%)	35000 (49.8%)	41400 (12.1%)	33900 (22.2%)
Cycle 3 Day 1 (n=2,1,1,0,0,2,5)	65100 (13.9%)	50500	47700			54500 (27.4%)	60900 (38.9%)

Maximum observed serum concentration (Cmax) of LAG525

Description	PK parameters were calculated based on LAG525 serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the LAG525 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received LAG525 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**

Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	8	3	7	4	8	14
Maximum observed serum concentration (Cmax) of LAG525 (units: µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=7,8,3,7,4,8,14)	166 (28.1%)	209 (29.0%)	202 (21.0%)	157 (23.4%)	229 (40.1%)	232 (35.2%)	233 (25.5%)
Cycle 3 Day 1 (n=2,2,1,2,0,3,5)	298 (110.0%)	209 (23.6%)	260	184 (18.5%)		263 (29.1%)	257 (31.0%)

Time to reach maximum serum concentration (Tmax) of LAG525

Description	PK parameters were calculated based on LAG525 serum concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the LAG525 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received LAG525 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525	**Spartalizumab 400mgQ4W +LAG525**	**Spartalizumab 400mgQ4W +LAG525**	**Spartalizumab 400mgQ4W +LAG525**	**Spartalizumab 400mgQ4W +LAG525**	**Spartalizumab 400mgQ4W +LAG525**	**Spartalizumab 400mgQ4W +LAG525**

	600mgQ4W +NIR178 80mgBID	600mgQ4W +NIR178 160mgBID	600mgQ4W +NIR178 240mgBID	600mgQ4W +capmatinib 200mgBID	600mgQ4W +capmatinib 300mgBID	600mgQ4W +MCS110 5mg/kgQ4W	600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	8	3	7	4	8	14
Time to reach maximum serum concentration (Tmax) of LAG525 (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n=7,8,3,7,4,8,14)	0.567 (0.5 to 0.917)	0.633 (0.5 to 1.95)	0.617 (0.567 to 0.7)	0.567 (0.5 to 1.07)	0.517 (0.5 to 0.6)	0.575 (0.5 to 0.917)	0.592 (0.5 to 1.08)
Cycle 3 Day 1 (n=2,2,1,2,0,3,5)	0.667 (0.583 to 0.75)	0.65 (0.583 to 0.717)	0.683 (0.683 to 0.683)	0.525 (0.5 to 0.55)		0.567 (0.5 to 0.667)	0.6 (0.55 to 0.85)

Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of LAG525

Description	PK parameters were calculated based on LAG525 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the LAG525 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received LAG525 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	11	3	8	4	9	15
Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of LAG525 (units: hr*µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=7,11,3,8,4,9,15)	44900 (52.9%)	52900 (32.1%)	54100 (21.3%)	45200 (26.1%)	63000 (26.6%)	53900 (31.3%)	61800 (23.2%)
Cycle 3 Day 1 (n=2,2,1,2,0,3,5)	113000 (35.0%)	56200 (14.9%)	57400	49900 (21.3%)		82000 (54.8%)	86200 (44.1%)

Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of LAG525

Description: PK parameters were calculated based on LAG525 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC0-672 calculation.

Time Frame: pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the LAG525 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.

Analysis Population Description: Patients in the pharmacokinetic analysis set (PAS) who received LAG525 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	5	9	3	3	2	5	14
Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of LAG525 (units: hr*µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=5,9,3,3,2,5,14)	52000 (34.5%)	52600 (34.5%)	54100 (21.1%)	45700 (41.9%)	69400 (42.2%)	67900 (15.3%)	61200 (23.1%)
Cycle 3 Day 1 (n=1,1,1,0,0,3,4)	143000	62400	57400			82000 (54.7%)	92600 (44.8%)

Maximum observed plasma concentration (Cmax) of NIR178

Description	PK parameters were calculated based on NIR178 plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after NIR178 dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)
Number of Participants Analyzed [units: participants]	7	11	3
Maximum observed plasma concentration (Cmax) of NIR178 (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=7,11,3)	26.9 (202.7%)	77.2 (476.7%)	632 (459.2%)
Cycle 3 Day 1 (n=2,2,0)	33.4 (282.5%)	13.5 (39.3%)	

Time to reach maximum plasma concentration (Tmax) of NIR178

Description	PK parameters were calculated based on NIR178 plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after NIR178 dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)
Number of Participants Analyzed [units: participants]	7	11	3
Time to reach maximum plasma concentration (Tmax) of NIR178 (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n=7,11,3)	2 (2 to 7.5)	2 (0.583 to 4.08)	3.53 (1.88 to 4)
Cycle 3 Day 1 (n=2,2,0)	3 (2 to 4)	2.28 (0.583 to 3.97)	

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NIR178

Description	PK parameters were calculated based on NIR178 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after NIR178 dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)

Number of Participants Analyzed [units: participants]	7	11	3
Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NIR178 (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=7,11,3)	62.7 (403.3%)	215 (486.5%)	2120 (356.0%)
Cycle 3 Day 1 (n=2,2,0)	101 (203.4%)	42.5 (143.6%)	

Area under the plasma concentration-time curve from time zero to 8 hours (AUC0-8) of NIR178

Description	PK parameters were calculated based on NIR178 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC0-8 calculation.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after NIR178 dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)
Number of Participants Analyzed [units: participants]	2	3	0
Area under the plasma concentration-time curve from time zero to 8 hours (AUC0-8) of NIR178 (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=2,3,0)	134 (73.6%)	157 (437.5%)	
Cycle 3 Day 1 (n=0,1,0)		22.7	

Maximum observed plasma concentration (Cmax) of capmatinib

Description	PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after capmatinib dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received capmatinib and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**
Arm/Group Description	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)
Number of Participants Analyzed [units: participants]	8	5
Maximum observed plasma concentration (Cmax) of capmatinib (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=8,5)	1380 (155.0%)	3030 (37.4%)
Cycle 3 Day 1 (n=2,1)	1970 (33.7%)	1740

Time to reach maximum plasma concentration (Tmax) of capmatinib

Description	PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after capmatinib dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received capmatinib and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID
Arm/Group Description	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)
Number of Participants Analyzed [units: participants]	8	5
Time to reach maximum plasma concentration (Tmax) of capmatinib (units: hours)	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n=8,5)	1.08 (1 to 4)	2.13 (0.5 to 4.22)
Cycle 3 Day 1 (n=2,1)	0.817 (0.583 to 1.05)	1.05 (1.05 to 1.05)

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of capmatinib

Description	PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after capmatinib dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received capmatinib and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID
Arm/Group Description	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)
Number of Participants Analyzed [units: participants]	8	5
Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**

capmatinib (units: hr*ng/mL)		
Cycle 1 Day 1 (n=8,5)	4990 (126.5%)	11400 (47.2%)
Cycle 3 Day 1 (n=2,1)	6660 (30.3%)	7260

Area under the plasma concentration-time curve from time zero to 8 hours (AUC0-8) of capmatinib

Description	PK parameters were calculated based on capmatinib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC0-8 calculation.
Time Frame	pre-dose, 0.5, 1, 2, 4 and 8 hours after capmatinib dosing on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received capmatinib and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**
Arm/Group Description	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)
Number of Participants Analyzed [units: participants]	7	5
Area under the plasma concentration-time curve from time zero to 8 hours (AUC0-8) of capmatinib (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=7,5)	5080 (143.6%)	14300 (48.1%)
Cycle 3 Day 1 (n=2,1)	6720 (31.6%)	7350

Maximum observed serum concentration (Cmax) of MCS110

Description	PK parameters were calculated based on MCS110 serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.

Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the MCS110 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received MCS110 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W
Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)
Number of Participants Analyzed [units: participants]	8
Maximum observed serum concentration (Cmax) of MCS110 (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=8)	119000 (30.0%)
Cycle 3 Day 1 (n=3)	103000 (96.2%)

Time to reach maximum serum concentration (Tmax) of MCS110

Description	PK parameters were calculated based on MCS110 serum concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the MCS110 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received MCS110 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W
Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)

Number of Participants Analyzed [units: participants]	8
Time to reach maximum serum concentration (Tmax) of MCS110 (units: hours)	**Median (Full Range)**
Cycle 1 Day 1 (n=8)	0.975 (0.5 to 1.25)
Cycle 3 Day 1 (n=3)	1.02 (0.5 to 141)

Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of MCS110

Description	PK parameters were calculated based on MCS110 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the MCS110 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received MCS110 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W
Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)
Number of Participants Analyzed [units: participants]	9
Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of MCS110 (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=9)	20400000 (37.2%)
Cycle 3 Day 1 (n=3)	23000000 (42.7%)

Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of MCS110

Description	PK parameters were calculated based on MCS110 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC0-672 calculation.
Time Frame	pre-infusion, end of infusion and 168, 336 and 672 hours after completion of the MCS110 infusion on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of the infusion was approximately 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received MCS110 and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W
Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)
Number of Participants Analyzed [units: participants]	4
Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of MCS110 (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=4)	27100000 (18.7%)
Cycle 3 Day 1 (n=1)	29000000

Maximum observed serum concentration (Cmax) of canakinumab

Description	PK parameters were calculated based on canakinumab serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	pre-injection, 168, 336 and 672 hours after canakinumab injection on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received canakinumab and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	15
Maximum observed serum concentration (Cmax) of canakinumab (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=15)	49300 (37.7%)
Cycle 3 Day 1 (n=5)	81800 (50.0%)

Time to reach maximum serum concentration (Tmax) of canakinumab

Description	PK parameters were calculated based on canakinumab serum concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) concentration following a dose. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-injection, 168, 336 and 672 hours after canakinumab injection on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received canakinumab and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	15
Time to reach maximum serum concentration (Tmax) of canakinumab (units: hours)	**Median (Full Range)**
Cycle 1 Day 1 (n=15)	168 (163 to 335)
Cycle 3 Day 1 (n=5)	165 (161 to 336)

Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of canakinumab

Description	PK parameters were calculated based on canakinumab serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-injection, 168, 336 and 672 hours after canakinumab injection on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received canakinumab and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	15
Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of canakinumab (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=15)	22500000 (47.4%)
Cycle 3 Day 1 (n=5)	33400000 (67.2%)

Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of canakinumab

Description	PK parameters were calculated based on canakinumab serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC0-672 calculation.
Time Frame	pre-injection, 168, 336 and 672 hours after canakinumab injection on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received canakinumab and had an available value for the outcome measure in each timepoint. PAS consists of all patients who received one of the planned treatments and provided at least one primary PK parameter.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	6
Area under the serum concentration-time curve from time zero to 672 hours (AUC0-672) of canakinumab (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=6)	22600000 (27.6%)
Cycle 3 Day 1 (n=1)	19000000

Number of participants with anti-PDR001 antibodies

Description	Immunogenicity was evaluated in serum by using a validated enzyme-linked immunosorbent assay (ELISA) method. Patient ADA status was defined as follows: • ADA-negative at baseline: ADA-negative sample at baseline • ADA-positive at baseline: ADA-positive sample at baseline • ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline determinant sample, all of which are ADA-negative samples • Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive = ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample • Treatment-reduced ADA-positive= ADA-positive sample at baseline and at least one post baseline determinant sample, all of which are ADA-negative samples
Time Frame	Baseline (before first dose) and post-baseline (from first dose to 150 days after last dose, up to 3.8 years (Arm 1), 0.8 years (Arm 2), 3.6 years (Arm 3) and 3.1 years (Arm 4))
Analysis Population Description	All patients who received at least one dose of PDR001 with a non-missing baseline ADA sample or at least one non-missing post-baseline ADA sample.

Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W

Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	11	3	8	4	8	16
Number of participants with anti-PDR001 antibodies (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
ADA-negative at baseline	6 (85.71%)	11 (100%)	3 (100%)	8 (100%)	4 (100%)	8 (100%)	16 (100%)
ADA-positive at baseline	1 (14.29%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
ADA-negative post-baseline	5 (71.43%)	11 (100%)	3 (100%)	6 (75%)	4 (100%)	7 (87.5%)	12 (75%)
Treatment-induced ADA-positive	1 (14.29%)	0 (%)	0 (%)	2 (25%)	0 (%)	1 (12.5%)	4 (25%)
Treatment-boosted ADA-positive	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Treatment-reduced ADA-positive	1 (14.29%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Number of participants with anti-LAG525 antibodies

Description

Immunogenicity was evaluated in serum by using a validated enzyme-linked immunosorbent assay (ELISA) method. Patient ADA status was defined as follows: • ADA-negative at baseline: ADA-negative sample at baseline • ADA-positive at baseline: ADA-positive sample at baseline • ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline determinant sample, all of which are ADA-negative samples • Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive = ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample •

Treatment-reduced ADA-positive= ADA-positive sample at baseline and at least one post baseline determinant sample, all of which are ADA-negative samples

Time Frame: Baseline (before first dose) and post-baseline (from first dose to 150 days after last dose, up to 3.8 years (Arm 1), 0.8 years (Arm 2), 3.6 years (Arm 3) and 3.1 years (Arm 4))

Analysis Population Description: All patients who received at least one dose of LAG525 with a non-missing baseline ADA sample or at least one non-missing post-baseline ADA sample.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	3	8	4	8	16
Number of participants with anti-LAG525 antibodies (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
ADA-negative at baseline	6 (85.71%)	11 (91.67%)	3 (100%)	8 (100%)	4 (100%)	8 (100%)	16 (100%)
ADA-positive at baseline	1 (14.29%)	1 (8.33%)	0 (%)	0 (%)	0 (%)	8 (100%)	0 (%)

ADA-negative post-baseline	5 (71.43%)	10 (83.33%)	3 (100%)	7 (87.5%)	4 (100%)	8 (100%)	15 (93.75%)
Treatment-induced ADA-positive	1 (14.29%)	1 (8.33%)	0 (%)	1 (12.5%)	0 (%)	0 (%)	1 (6.25%)
Treatment-boosted ADA-positive	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Treatment-reduced ADA-positive	1 (14.29%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Number of participants with anti-MCS110 antibodies

Description	Immunogenicity was evaluated in serum by using a validated enzyme-linked immunosorbent assay (ELISA) method. Patient ADA status was defined as follows: • ADA-negative at baseline: ADA-negative sample at baseline • ADA-positive at baseline: ADA-positive sample at baseline • ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline determinant sample, all of which are ADA-negative samples • Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive = ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample • Treatment-reduced ADA-positive= ADA-positive sample at baseline and at least one post baseline determinant sample, all of which are ADA-negative samples
Time Frame	Baseline (before first dose) and post-baseline (from first dose to 150 days after last dose, up to 3.6 years (Arm 3))
Analysis Population Description	All patients who received at least one dose of MCS110 with a non-missing baseline ADA sample or at least one non-missing post-baseline ADA sample.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W
Arm/Group Description	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)
Number of Participants Analyzed [units: participants]	8
Number of participants with anti-MCS110 antibodies (units: participants)	**Count of Participants (Percentage)**
ADA-negative at baseline	8 (100%)

ADA-positive at baseline	0 (%)
ADA-negative post-baseline	8 (100%)
Treatment-induced ADA-positive	0 (%)
Treatment-boosted ADA-positive	0 (%)
Treatment-reduced ADA-positive	0 (%)

Number of participants with anti-canakinumab antibodies

Description	Immunogenicity was evaluated in serum by using a validated enzyme-linked immunosorbent assay (ELISA) method. Patient ADA status was defined as follows: • ADA-negative at baseline: ADA-negative sample at baseline • ADA-positive at baseline: ADA-positive sample at baseline • ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline determinant sample, all of which are ADA-negative samples • Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive = ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample • Treatment-reduced ADA-positive= ADA-positive sample at baseline and at least one post baseline determinant sample, all of which are ADA-negative samples
Time Frame	Baseline (before first dose) and post-baseline (from first dose to 150 days after last dose, up to 3.1 years (Arm 4))
Analysis Population Description	All patients who received at least one dose of canakinumab with a non-missing baseline ADA sample or at least one non-missing post-baseline ADA sample.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	16
Number of participants with anti-canakinumab antibodies (units: participants)	**Count of Participants (Percentage)**

ADA-negative at baseline	16 (100%)
ADA-positive at baseline	0 (%)
ADA-negative post-baseline	16 (100%)
Treatment-induced ADA-positive	0 (%)
Treatment-boosted ADA-positive	0 (%)
Treatment-reduced ADA-positive	0 (%)

Best Overall Response (BOR) per RECIST v1.1

Description	BOR is defined as the best response recorded from the start of the study treatment until disease progression/recurrence, based on local investigator assessment per RECIST v1.1. However, any assessments taken more than 30 days after the last dose of study therapy were not included in the best overall response derivation. Complete Response (CR) and Partial response (PR) per RECIST v1.1 had to be confirmed by a new assessment after at least 4 weeks.
Time Frame	From start of treatment until disease progression, assessed up to 3.5 years (Arm 1), 0.5 years (Arm 2), 3.3 years (Arm 3) and 2.8 years (Arm 4)
Analysis Population Description	All patients who received any study drug

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525	Arm 1: spartalizumab + LAG525	Arm 1: spartalizumab + LAG525	Arm 2: spartalizumab + LAG525	Arm 2: spartalizumab + LAG525	Arm 3: spartalizumab + LAG525	Arm 4: spartalizumab + LAG525

	(backbone) in combination with NIR178 80 mg BID (partner)	(backbone) in combination with NIR178 160 mg BID (partner)	(backbone) in combination with NIR178 240 mg BID (partner)	(backbone) in combination with capmatinib 200 mg BID (partner)	(backbone) in combination with capmatinib 300 mg BID (partner)	(backbone) in combination with MCS110 5 mg/kg Q4W (partner)	(backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Best Overall Response (BOR) per RECIST v1.1 (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
Complete Response (CR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (10%)	1 (5.88%)
Partial Response (PR)	2 (28.57%)	2 (16.67%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Stable Disease (SD)	2 (28.57%)	3 (25%)	1 (20%)	1 (12.5%)	0 (%)	2 (20%)	4 (23.53%)
Progressive Disease (PD)	2 (28.57%)	6 (50%)	4 (80%)	5 (62.5%)	4 (80%)	7 (70%)	9 (52.94%)
Not evaluable (NE)	1 (14.29%)	1 (8.33%)	0 (%)	2 (25%)	1 (20%)	0 (%)	3 (17.65%)

Best Overall Response (BOR) per iRECIST

Description	BOR is defined as the best response recorded from the start of the study treatment until disease progression/recurrence, based on local investigator assessment per iRECIST. However, any assessments taken more than 30 days after the last dose of study therapy were not included in the best overall response derivation. Complete Response (iCR) and Partial response (iPR) per iRECIST had to be confirmed by a new assessment after at least 4 weeks. Also, disease progression, as per iRECIST, had to be confirmed after at least 4 weeks.
Time Frame	From start of treatment until disease progression, assessed up to 3.5 years (Arm 1), 0.5 years (Arm 2), 3.3 years (Arm 3) and 2.8 years (Arm 4)
Analysis Population Description	All patients who received any study drug

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	7	12	5	8	5	10	17
Best Overall Response (BOR) per iRECIST (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
Complete Response (iCR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (10%)	1 (5.88%)
Partial Response (iPR)	2 (28.57%)	1 (8.33%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Stable Disease (iSD)	2 (28.57%)	0 (%)	1 (20%)	1 (12.5%)	0 (%)	2 (20%)	4 (23.53%)
Unconfirmed Progressive Disease (iUPD)	2 (28.57%)	5 (41.67%)	2 (40%)	2 (25%)	3 (60%)	4 (40%)	6 (35.29%)
Confirmed Progressive Disease (iCPD)	0 (%)	2 (16.67%)	0 (%)	0 (%)	0 (%)	1 (10%)	1 (5.88%)
Not evaluable (NE)	1 (14.29%)	4 (33.33%)	2 (40%)	5 (62.5%)	2 (40%)	2 (20%)	5 (29.41%)

NOVARTIS

Progression-Free Survival (PFS) per RECIST v1.1

Description	PFS is defined as the time from the date of start of treatment to the date of the first documented progression or death due to any cause. If a patient did not have an event, PFS was censored at the date of the last adequate tumor assessment. Tumor response was based on local investigator assessment per RECIST v1.1. PFS was analyzed using Kaplan-Meier estimates only for the groups of size ≥ 10 patients treated at the Maximum Tolerated Dose (MTD)/Recommended Dose for Expansion (RDE).
Time Frame	From start of treatment until disease progression or death due to any cause, assessed up to 3.5 years (Arm 1) and 2.8 years (Arm 4)
Analysis Population Description	All treatment groups of size ≥ 10 patients treated at the Maximum Tolerated Dose (MTD)/Recommended Dose for Expansion (RDE). The MTD/RDE was only determined for Arm 1 and 4 and therefore Arm 2 and 3 were not part of this analysis.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	12	17
Progression-Free Survival (PFS) per RECIST v1.1 (units: months)	**Median (90% Confidence Interval)**	**Median (90% Confidence Interval)**
	1.9 (1.2 to 10.0)	1.9 (1.4 to 8.2)

Progression-Free Survival (iPFS) per iRECIST

Description	iPFS is defined as the time from the date of start of treatment to the date of the first documented progression or death due to any cause. If a patient did not have an event, PFS was censored at the date of the last adequate tumor assessment. Tumor response was based on local investigator assessment per iRECIST. iPFS was analyzed using Kaplan-Meier estimates only for the groups of size ≥ 10 patients treated at the Maximum Tolerated Dose (MTD)/Recommended Dose for Expansion (RDE).
Time Frame	From start of treatment until disease progression or death due to any cause, assessed up to 3.5 years (Arm 1) and 2.8 years (Arm 4)
Analysis Population Description	All treatment groups of size ≥ 10 patients treated at the Maximum Tolerated Dose (MTD)/Recommended Dose for Expansion (RDE). The MTD/RDE was only determined for Arm 1 and 4 and therefore Arm 2 and 3 were not part of this analysis.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	12	17
Progression-Free Survival (iPFS) per iRECIST (units: months)	**Median (90% Confidence Interval)**	**Median (90% Confidence Interval)**
	1.7 (1.1 to 3.5)	2.1 (1.4 to 8.2)

Change from baseline in PD-L1 expression in tumor tissue from SP142 assay

Description	The tumor expression of programmed cell death-ligand 1 (PD-L1) was measured by immunohistochemical (IHC) methods. This record summarizes the PD-L1 expression in tumor tissue obtained with Ventana PD-L1 (SP142) assay. Newly obtained pre- and on-treatment paired tumor samples were required and collected at the screening and on-treatment from the same lesion if safe and medically feasible. If an on-treatment biopsy was not collected from the same lesion as in the pre-treatment biopsy, then a tumor sample from another lesion was considered acceptable.
Time Frame	Screening and on-treatment (Cycle 2 Day 1 or Day 15). The duration of one cycle was 28 days.
Analysis Population Description	All patients who received any study drug, had newly obtained pre- and on-treatment paired tumor samples and had a valid assessment for the outcome measure.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination	Arm 1: spartalizumab + LAG525 (backbone) in combination	Arm 1: spartalizumab + LAG525 (backbone) in combination	Arm 2: spartalizumab + LAG525 (backbone) in combination	Arm 2: spartalizumab + LAG525 (backbone) in combination	Arm 3: spartalizumab + LAG525 (backbone) in combination	Arm 4: spartalizumab + LAG525 (backbone) in combination

	with NIR178 80 mg BID (partner)	with NIR178 160 mg BID (partner)	with NIR178 240 mg BID (partner)	with capmatinib 200 mg BID (partner)	with capmatinib 300 mg BID (partner)	with MCS110 5 mg/kg Q4W (partner)	with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	3	4	1	1	2	4	5
Change from baseline in PD-L1 expression in tumor tissue from SP142 assay (units: percentage positive immune cells (IC%))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	-1.0 ± 3.00	-1.9 ± 10.71	0.0	9.5	2.3 ± 3.89	1.4 ± 1.80	0.8 ± 1.15

Change from baseline in PD-L1 expression in tumor tissue from Ventana 22c3 assay expressed as PPT

Description	The tumor expression of PD-L1 was measured by immunohistochemical (IHC) methods. This record summarizes the PD-L1 expression in tumor tissue obtained with Ventana 22c3 assay and expressed as percentage positive tumor cells (PPT). Newly obtained pre- and on-treatment paired tumor samples were required and collected at the screening and on-treatment from the same lesion if safe and medically feasible. If an on-treatment biopsy was not collected from the same lesion as in the pre-treatment biopsy, then a tumor sample from another lesion was considered acceptable.
Time Frame	Screening and on-treatment (Cycle 2 Day 1 or Day 15). The duration of one cycle was 28 days.
Analysis Population Description	All patients who received any study drug, had newly obtained pre- and on-treatment paired tumor samples and had a valid assessment for the outcome measure.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W**
Arm/Group Description	Arm 1: spartalizumab +	Arm 1: spartalizumab +	Arm 1: spartalizumab +	Arm 2: spartalizumab +	Arm 2: spartalizumab +	Arm 3: spartalizumab +	Arm 4: spartalizumab +

	LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	3	4	1	1	2	4	6
Change from baseline in PD-L1 expression in tumor tissue from Ventana 22c3 assay expressed as PPT (units: percentage positive tumor cells (PPT))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	0.0 ± 0.00	-2.4 ± 12.09	0.0	30.0	0.0 ± 0.00	1.5 ± 2.35	4.1 ± 5.97

Change from baseline in PD-L1 expression in tumor tissue from Ventana 22c3 assay expressed as CPS

Description	The tumor expression of PD-L1 was measured by immunohistochemical (IHC) methods. This record summarizes the PD-L1 expression in tumor tissue obtained with Ventana 22c3 assay and expressed as combined positivity score (CPS). CPS is calculated by the number of PD-L1 positive cells, including tumor cells, lymphocytes and macrophages, divided by the total number of viable tumor cells and multiplied by 100 (range 0-100). Newly obtained pre- and on-treatment paired tumor samples were required and collected at the screening and on-treatment from the same lesion if safe and medically feasible. If an on-treatment biopsy was not collected from the same lesion as in the pre-treatment biopsy, then a tumor sample from another lesion was considered acceptable.
Time Frame	Screening and on-treatment (Cycle 2 Day 1 or Day 15). The duration of one cycle was 28 days.
Analysis Population Description	All patients who received any study drug, had newly obtained pre- and on-treatment paired tumor samples and had a valid assessment for the outcome measure.

Spartalizumab 400mgQ4W +LAG525 600mgQ4W	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W**

	+NIR178 80mgBID	+NIR178 160mgBID	+NIR178 240mgBID	+capmatinib 200mgBID	+capmatinib 300mgBID	+MCS110 5mg/kgQ4W	+canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	3	4	1	1	2	4	6
Change from baseline in PD-L1 expression in tumor tissue from Ventana 22c3 assay expressed as CPS (units: combined positivity score (CPS))	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	0.7 ± 17.93	1.9 ± 14.79	-2.0	48.0	1.0 ± 33.94	7.1 ± 3.33	15.0 ± 19.31

Change from baseline in CD8 percent marker area in tumor tissue

Description	The tumor expression of CD8 was measured by immunohistochemical (IHC) methods. Newly obtained pre- and on-treatment paired tumor samples were required and collected at the screening and on-treatment from the same lesion if safe and medically feasible. If an on-treatment biopsy was not collected from the same lesion as in the pre-treatment biopsy, then a tumor sample from another lesion was considered acceptable.
Time Frame	Screening and on-treatment (Cycle 2 Day 1 or Day 15). The duration of one cycle was 28 days.
Analysis Population Description	All patients who received any study drug, had newly obtained pre- and on-treatment paired tumor samples and had a valid assessment for the outcome measure.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	4	4	1	1	2	4	5
Change from baseline in CD8 percent marker area in tumor tissue (units: CD8 percent marker area)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	2.5 ± 5.04	1.9 ± 4.07	0.0	7.5	1.2 ± 3.04	0.4 ± 0.18	2.6 ± 6.01

Change from baseline in LAG3 percent marker area in tumor tissue

Description	The tumor expression of lymphocyte-activation gene-3 (LAG3) was measured by immunohistochemical (IHC) methods. Newly obtained pre- and on-treatment paired tumor samples were required and collected at the screening and on-treatment from the same lesion if safe and medically feasible. If an on-treatment biopsy was not collected from the same lesion as in the pre-treatment biopsy, then a tumor sample from another lesion was considered acceptable.
Time Frame	Screening and on-treatment (Cycle 2 Day 1 or Day 15). The duration of one cycle was 28 days.
Analysis Population Description	All patients who received any study drug, had newly obtained pre- and on-treatment paired tumor samples and had a valid assessment for the outcome measure.

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Number of Participants Analyzed [units: participants]	3	4	1	1	2	3	5
Change from baseline in LAG3 percent marker area in tumor tissue (units: LAG3 percent marker area)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	2.6 ± 1.96	2.7 ± 9.15	0.0	8.0	0.9 ± 1.56	1.0 ± 0.92	1.5 ± 2.51

Safety Results

Time Frame	Adverse events were collected from first dose of study treatment to 150 days after last dose, up to 3.8 years (Arm 1), 0.8 years (Arm 2), 3.6 years (Arm 3) and 3.1 years (Arm 4).
Additional Description	Any sign or symptom that occurs during the on-treatment and safety follow-up period.

Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID N = 7	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID N = 12**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID N = 5**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID N = 8**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID N = 5**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W N = 10**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W N = 17**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Total Number Affected	2	4	4	3	5	3	9
Total Number At Risk	7	12	5	8	5	10	17

Serious Adverse Events

Time Frame	Adverse events were collected from first dose of study treatment to 150 days after last dose, up to 3.8 years (Arm 1), 0.8 years (Arm 2), 3.6 years (Arm 3) and 3.1 years (Arm 4).
Additional Description	Any sign or symptom that occurs during the on-treatment and safety follow-up period.
Source Vocabulary for Table Default	MedDRA (25.1)
Collection Approach for Table Default	Systematic Assessment

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID N = 7	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID N = 12**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID N = 5**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID N = 8**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID N = 5**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W N = 10**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W N = 17**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Total # Affected by any Serious Adverse Event	2	6	2	4	4	4	10
Total # at Risk by any Serious Adverse Event	7	12	5	8	5	10	17
Blood and lymphatic system disorders							

Febrile neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Cardiac disorders							
Supraventricular tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Eye disorders							
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Gastrointestinal disorders							
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Constipation	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diarrhoea	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Pancreatitis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancreatitis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
General disorders and administration site conditions							
General physical health deterioration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Mucosal inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Multiple organ dysfunction syndrome	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	1 (5.88%)
Hepatobiliary disorders							
Autoimmune hepatitis	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Cholangitis	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic function abnormal	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertransaminasaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations							
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Pneumonia bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Injury, poisoning and procedural complications							
Hip fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Infusion related reaction	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Jaw fracture	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations							
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic enzyme increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders							
Decreased appetite	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Diabetic ketoacidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)

Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Musculoskeletal and connective tissue disorders							
Arthralgia	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Muscular weakness	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polyarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Tumour haemorrhage	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders							
Myasthenia gravis	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neuralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Polyneuropathy in malignant disease	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Spinal cord compression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Pregnancy, puerperium and perinatal conditions							
Pregnancy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Psychiatric disorders							
Delirium	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Renal and urinary disorders							
Hydronephrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)

Reproductive system and breast disorders							
Breast pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Respiratory, thoracic and mediastinal disorders							
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Pneumonitis	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders							
Rash	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Urticaria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders							
Embolism	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events were collected from first dose of study treatment to 150 days after last dose, up to 3.8 years (Arm 1), 0.8 years (Arm 2), 3.6 years (Arm 3) and 3.1 years (Arm 4).
Additional Description	Any sign or symptom that occurs during the on-treatment and safety follow-up period.
Source Vocabulary for Table Default	MedDRA (25.1)

NOVARTIS

Collection Approach for Table Default Systematic Assessment

Frequent Event Reporting Threshold 5%

	Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 80mgBID N = 7	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 160mgBID N = 12**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +NIR178 240mgBID N = 5**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 200mgBID N = 8**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +capmatinib 300mgBID N = 5**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +MCS110 5mg/kgQ4W N = 10**	**Spartalizumab 400mgQ4W +LAG525 600mgQ4W +canakinumab 600mgQ8W N = 17**
Arm/Group Description	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 80 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 160 mg BID (partner)	Arm 1: spartalizumab + LAG525 (backbone) in combination with NIR178 240 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 200 mg BID (partner)	Arm 2: spartalizumab + LAG525 (backbone) in combination with capmatinib 300 mg BID (partner)	Arm 3: spartalizumab + LAG525 (backbone) in combination with MCS110 5 mg/kg Q4W (partner)	Arm 4: spartalizumab + LAG525 (backbone) in combination with canakinumab 600 mg Q8W (partner)
Total # Affected by any Other Adverse Event	7	12	4	8	5	10	16
Total # at Risk by any Other Adverse Event	7	12	5	8	5	10	17
Blood and lymphatic system disorders							
Anaemia	1 (14.29%)	3 (25.00%)	1 (20.00%)	4 (50.00%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Leukocytosis	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Leukopenia	1 (14.29%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	2 (20.00%)	0 (0.00%)
Lymphopenia	0 (0.00%)	1 (8.33%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders							
Sinus tachycardia	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Supraventricular tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear and labyrinth disorders							
Paraesthesia ear	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tinnitus	0 (0.00%)	2 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vertigo	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Endocrine disorders							
Autoimmune thyroiditis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Hyperthyroidism	0 (0.00%)	3 (25.00%)	1 (20.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hypothyroidism	0 (0.00%)	4 (33.33%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	2 (11.76%)
Immune-mediated thyroiditis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Eye disorders							
Blepharitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)
Conjunctival haemorrhage	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diplopia	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Lacrimation decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Ophthalmoplegia	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Periorbital oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (30.00%)	0 (0.00%)
Swelling of eyelid	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Gastrointestinal disorders							
Abdominal distension	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain	3 (42.86%)	2 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Constipation	1 (14.29%)	6 (50.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	3 (17.65%)
Dental caries	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Diarrhoea	2 (28.57%)	2 (16.67%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	1 (10.00%)	2 (11.76%)
Dry mouth	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Dyspepsia	0 (0.00%)	2 (16.67%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	2 (20.00%)	1 (5.88%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Flatulence	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	3 (42.86%)	2 (16.67%)	2 (40.00%)	4 (50.00%)	0 (0.00%)	2 (20.00%)	6 (35.29%)
Oral discomfort	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancreatitis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Salivary duct inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Stomatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Toothache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Vomiting	1 (14.29%)	2 (16.67%)	1 (20.00%)	4 (50.00%)	2 (40.00%)	1 (10.00%)	2 (11.76%)
General disorders and administration site conditions							
Asthenia	2 (28.57%)	2 (16.67%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	6 (60.00%)	1 (5.88%)

Axillary pain	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Chest pain	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chills	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Face oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Facial pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Fatigue	2 (28.57%)	3 (25.00%)	0 (0.00%)	2 (25.00%)	1 (20.00%)	1 (10.00%)	4 (23.53%)
Influenza like illness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Malaise	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mucosal inflammation	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Oedema peripheral	0 (0.00%)	1 (8.33%)	1 (20.00%)	3 (37.50%)	1 (20.00%)	0 (0.00%)	1 (5.88%)
Pain	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Peripheral swelling	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	2 (28.57%)	1 (8.33%)	2 (40.00%)	1 (12.50%)	2 (40.00%)	3 (30.00%)	1 (5.88%)
Hepatobiliary disorders							
Autoimmune hepatitis	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic function abnormal	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hepatic steatosis	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertransaminasaemia	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders							
Hypersensitivity	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations							
Biliary tract infection	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Conjunctivitis	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
COVID-19	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Cystitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Folliculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Herpes zoster	1 (14.29%)	1 (8.33%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Influenza	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Klebsiella infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Nasal herpes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Oral candidiasis	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (17.65%)
Oral herpes	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Paronychia	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Periodontitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Pharyngotonsillitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Pneumonia bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Rash pustular	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sinusitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Streptococcal bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Vulvovaginal candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Wound infection	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications							
Jaw fracture	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Procedural pain	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Investigations							
Alanine aminotransferase increased	2 (28.57%)	4 (33.33%)	2 (40.00%)	3 (37.50%)	1 (20.00%)	3 (30.00%)	3 (17.65%)
Amylase increased	1 (14.29%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Aspartate aminotransferase increased	3 (42.86%)	3 (25.00%)	1 (20.00%)	3 (37.50%)	1 (20.00%)	6 (60.00%)	3 (17.65%)
Blood alkaline phosphatase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Blood bilirubin increased	0 (0.00%)	1 (8.33%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	2 (28.57%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (20.00%)	6 (60.00%)	2 (11.76%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood phosphorus increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	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%)	1 (5.88%)
Blood pressure increased	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood thyroid stimulating hormone increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Electrocardiogram QT interval	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Gamma-glutamyltransferase increased	1 (14.29%)	1 (8.33%)	1 (20.00%)	2 (25.00%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Haemoglobin decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hepatic enzyme increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (30.00%)	1 (5.88%)
Lymphocyte count decreased	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (5.88%)
Neutrophil count decreased	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
SARS-CoV-2 test negative	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	1 (10.00%)	1 (5.88%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Weight increased	1 (14.29%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
White blood cell count decreased	1 (14.29%)	0 (0.00%)	1 (20.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Metabolism and nutrition disorders							
Decreased appetite	1 (14.29%)	3 (25.00%)	0 (0.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	3 (17.65%)
Diabetes mellitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hyperglycaemia	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (17.65%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hyperlipidaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hypoalbuminaemia	1 (14.29%)	1 (8.33%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypocalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Hypokalaemia	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Hyponatraemia	0 (0.00%)	1 (8.33%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	2 (11.76%)

Musculoskeletal and connective tissue disorders							
Arthralgia	0 (0.00%)	2 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	3 (17.65%)
Back pain	0 (0.00%)	2 (16.67%)	1 (20.00%)	1 (12.50%)	0 (0.00%)	1 (10.00%)	3 (17.65%)
Bone pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Exostosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Flank pain	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Meniscopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Muscle spasms	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscular weakness	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal chest pain	0 (0.00%)	2 (16.67%)	0 (0.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	1 (5.88%)
Musculoskeletal pain	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	3 (17.65%)
Neck pain	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Osteoporosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	1 (5.88%)
Pain in jaw	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Polyarthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Spinal pain	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)							
Cancer pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancreatic cystadenoma	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)

Nervous system disorders							
Dizziness	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)
Dysgeusia	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	1 (14.29%)	2 (16.67%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	2 (20.00%)	1 (5.88%)
Hypoaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Lethargy	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Myasthenia gravis	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paraesthesia	0 (0.00%)	2 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral sensory neuropathy	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Restless legs syndrome	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sciatica	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Somnolence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Tremor	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders							
Anxiety	1 (14.29%)	1 (8.33%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Delirium	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Depression	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Insomnia	1 (14.29%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (17.65%)
Nervousness	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Restlessness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Renal and urinary disorders							
Bladder disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hydronephrosis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)

Pollakiuria	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Prerenal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Reproductive system and breast disorders							
Breast pain	0 (0.00%)	1 (8.33%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Pelvic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders							
Cough	1 (14.29%)	1 (8.33%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	3 (30.00%)	3 (17.65%)
Dysphonia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	1 (14.29%)	0 (0.00%)	0 (0.00%)	2 (25.00%)	1 (20.00%)	0 (0.00%)	1 (5.88%)
Hypoventilation	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasal congestion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)
Oropharyngeal pain	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (5.88%)
Pleural effusion	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonitis	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders							
Decubitus ulcer	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dry skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Erythema	0 (0.00%)	1 (8.33%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperhidrosis	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Palmar erythema	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pruritus	0 (0.00%)	1 (8.33%)	2 (40.00%)	3 (37.50%)	0 (0.00%)	3 (30.00%)	2 (11.76%)
Rash	1 (14.29%)	1 (8.33%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	4 (40.00%)	1 (5.88%)
Rash maculo-papular	0 (0.00%)	1 (8.33%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	3 (17.65%)
Rash pruritic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)

Skin lesion	1 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin tightness	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urticaria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders							
Deep vein thrombosis	1 (14.29%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Embolism	1 (14.29%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Flushing	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (5.88%)
Hot flush	0 (0.00%)	1 (8.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (11.76%)

Conclusion:

The safety profile was well characterized in all treatment arms evaluated in this study. Overall, the doses and combinations explored were manageable and no potential safety concerns were identified.

The PK of each agent was generally comparable with its PK as a single agent and there was no clear evidence of any pharmacokinetic drug-drug interaction. However, results should be interpreted with caution given limited data, particularly at steady state. Minimal on-treatment changes in CD8, LAG3, and PD-L1 (as measured in tissue by immunohistochemical methods) were observed in all four treatment arms, therefore no conclusions regarding increased immune cell infiltration can be drawn.

Modest antitumor effect was demonstrated in all four treatment arms evaluated in the study, however, due to limited data, no definitive conclusion could be drawn on efficacy for any of the individual treatment arms.

Date of Clinical Trial Report

27-Oct-2023