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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

LHC165 and PDR001 (spartalizumab)

Trial Indication(s)

Advanced malignancies

Protocol Number

CLHC165X2101

Protocol Title

A Phase I/Ib, open-label, multi-center dose-escalation and dose-expansion study of the safety and tolerability of intra-tumorally administered LHC165 single agent and in combination with PDR001 in patients with advanced malignancies

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1 (LHC165) and phase 3 (PDR001)

Study Start/End Dates

Study Start Date: January 31, 2018 (Actual)
Primary Completion Date: June 30, 2022 (Actual)
Study Completion Date: June 30, 2022 (Actual)

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Reason for Termination (If applicable)

Enrollment to the study was halted early during the dose expansion part, in February 2021, due to a low accrual rate and for business reasons. The enrolment halt was not as a consequence of any safety concerns. Patients in the study who in the Investigators' best judgement continued to derive benefit from PDR001 treatment were rolled over to the ongoing Novartis study CPDR001X2X01B for the continuation of their treatment after the end of CLHC165X2101 study.

Study Design/Methodology

This was a First-In-Human (FIH) Phase I/Ib, multi-center, open-label study of LHC165 as a single agent and in combination with PDR001 in patients with relapsed/refractory (R/R) solid tumors. The study consisted of two parts, a dose escalation part and a dose expansion part. Up to four groups in the escalation part and two groups in the expansion part were originally planned, to determine optimal single agent/combination schedule and maximum tolerated dose (MTD)/recommended dose for expansion (RDE).

Dose escalation groups:

- Group A: Single agent (LHC165) dose escalation group at a biweekly dosing interval.
- Group B: Single agent (LHC165) dose escalation group at a monthly dosing interval.
- Group C: An LHC165 in combination with PDR001 dose escalation group at a biweekly dosing interval for LHC165. PDR001 administered monthly.
- Group D: An LHC165 in combination with PDR001 dose escalation group at a monthly dosing interval for both LHC165 and PDR001.

As per protocol amendment 4, Groups B and D were not opened for enrolment. Based on the relatively short systemic half-life and limited biologic/clinical activity in the bi-weekly schedule, the monthly dosing scheduled is not expected to show biologic/clinic activity.

Dose expansion groups:

- Group E: A single agent (LHC165) dose expansion at the selected single agent MTD/RDE and dosing schedule in patients with head and neck squamous cell carcinoma (HNSCC), cutaneous melanoma, and other accessible tumors.

  This group was planned to be opened for enrollment based on the pharmacokinetics (PK), safety, and preliminary efficacy data observed in the dose escalation part. As per protocol amendment 4, Group E was not opened for enrolment.

- Group F: LHC165 600 µg bi-weekly in combination with PDR001 400 mg Q4W only in patients with HNSCC and cutaneous melanoma with accessible lesions.

Centers

9 centers in 7 countries: Japan(1), United States(2), Belgium(1), Italy(1), Spain(2), Korea, Republic of(1), Germany(1)

Objectives:

The primary objectives of the trial were:

- To characterize the safety and tolerability of intratumoral LHC165 in patients with solid tumors as a single agent and in combination with PDR001
- To determine and evaluate the maximum tolerated dose (MTD)/recommended dose (RD) for LHC165 as a single agent and in combination with PDR001

The following related primary endpoints were assessed:

  - Number of participants with Dose-Limiting Toxicities (DLTs) in Cycle 1
  - Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period
  - Number of participants with dose reductions and dose interruptions of LHC165 and PDR001

  - Dose intensity of LHC165 and PDR001

The secondary objectives were:

- To assess the preliminary anti-tumor activity of LHC165 as a single agent and in combination with PDR001. The following related endpoints were assessed:
  - Best Overall Response (BOR), Overall Response Rate (ORR), Disease Control Rate (DCR) and Duration of Response (DOR) per RECIST v1.1
  - Progression-Free Survival (PFS) per RECIST v1.1 (MTD/RDE only)
  - BOR, ORR, DCR and DOR per iRECIST
  - PFS per iRECIST (MTD/RDE only)
- To characterize the pharmacokinetics (PK) of LHC165 as a single agent and in combination with PDR001. The following related endpoints were assessed:
  - Cmax, AUCtau and AUCinf of LHC165 and PDR001
  - Number of participants with anti-drug antibodies (ADA) against PDR001
- To characterize the pharmacodynamic (PD) effect of LHC165 as a single agent and in combination with PDR001. The following related endpoints were assessed:
  - Percentage change from baseline of Tumor Infiltrating Lymphocytes (TILs) in injected lesions and non-injected lesions

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

For this study, the investigational drugs were LHC165 and PDR001. The study treatment was defined as LHC165 as a single agent or in combination with PDR001.

Group A – LHC165 single agent treatment in a biweekly dosing schedule

LHC165 as a single agent administered as intratumoral (IT) injections on Days 1 and 15 of a 28-day cycle for Cycles 1 and 2, followed by a two-cycle dosing pause (Cycles 3 and 4), and then repeat injections on Days 1 and 15 for Cycles 5 and 6. A total of eight injections of LHC165 administered over the course of six cycles of treatment. The initial dose was 100 µg LHC165 up to a maximum of 600 µg LHC165.

Group C – LHC165 in combination with PDR001 treatment in a biweekly dosing schedule

LHC165 administered as IT injections on Days 1 and 15 of a 28-day cycle for Cycles 1 and 2, followed by a two-cycle dosing pause (Cycles 3 and 4), and then repeat injections on Days 1 and 15 for Cycles 5 and 6. A total of eight injections of LHC165 administered over the course of six cycles of treatment. The initial dose was 100 µg LHC165 up to a maximum of 600 µg LHC165.

PDR001 fixed dose of 400 mg was administered by intravenous (i.v) infusion every 28 days, starting from Cycle 1 Day 1.

Group F – LHC165 in combination with PDR001 treatment dose expansion

The dose and dosing schedule of LHC165 in Group F was determined by the outcome of Groups A and C.

LHC165 600 µg bi-weekly was administered in combination with PDR001 400 mg Q4W as described previously.

Patients were treated until they experienced unacceptable toxicity, progressive disease per iRECIST, and/or treatment was discontinued at the discretion of the investigator, or the patient withdrew consent.

Statistical Methods

For the dose escalation of both single agent LHC165 and in combination with PDR001, the Bayesian hierarchical logistic regression model (BHLRM) was applied to estimate the relationship between dose and dose limiting toxicity (DLT) with overdose control (EWOC) principle. The goal was to identify the MTD/RD during the escalation part of both single agent and combination.

Tolerability was assessed by summarizing the number and percentage of patients with dose interruptions and dose reductions.

AEs were summarized by number and percentage of patients having at least one adverse event (AE). AEs in each primary System Organ Class (SOC) were listed for each Preferred Term (PT) using MedDRA coding. Adverse events and deaths were summarized by treatment groups.

Efficacy: BOR, ORR, and DCR per RECIST v1.1 and iRECIST were summarized by treatment group along with the corresponding 90% exact confidence intervals (CI). DOR was summarized by descriptive statistics. PFS was calculated with the Kaplan-Meier method.

The Pharmacokinetic Analysis Set (PAS) was used for all PK analyses. PK parameters were calculated by using non-compartmental methods.

Subject ADA status were assessed. Changes from baseline in CD8 biomarkers were summarized by descriptive statistics.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

• Written informed consent must be obtained prior to any procedures unless considered standard of care.
• Adult men and women (≥ 18 years of age) with histologically confirmed diagnosis of metastatic and/or advanced solid tumors not amenable to curative treatment by surgery.
• Patients must be willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up.
• Dose escalation: Patients with accessible tumors and with measurable disease as determined by RECIST 1.1 and have progressed despite standard treatment or are intolerant of standard treatment, or for whom no standard treatment exists.
• Dose expansion: Patients with advanced/metastatic solid tumors: HNSCC, melanoma, accessible tumors and visceral tumors (LHC165 combination with PDR001 only). Patients must have measurable disease as determined by RECIST 1.1 and have progressed despite standard treatment or are intolerant to standard treatment, or for whom no standard treatment exists• Patients must have at least two sites of disease amenable to biopsy.

• Patient has an Eastern Cooperative Oncology Group (ECOG) performance status 0-2.

Exclusion Criteria:
• Presence of symptomatic or uncontrolled central nervous system (CNS) metastases requiring local CNS-directed treatment.
• Patients diagnosed with hematological malignancies.
• Patients with prior stem cell transplants.
• Patients previously treated with TLR-7/8 agonist treatment.
• History of primary immunodeficiency
• Patients who discontinued prior anti-PD-1/PD-L1 therapy due to an anti-PD-1/PD-L1-related toxicity.
• Malignant disease, other than that being treated in this study

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Participant Flow Table

Overall Study

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg	Total
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	
Started	4	4	9	4	3	4	8	9	45
Completed	0	1	0	1	0	0	0	0	2
Not Completed	4	3	9	3	3	4	8	9	43
Progressive Disease	2	3	8	2	3	3	4	7	32
Patient Decision	1	0	1	0	0	0	2	0	4
Adverse Event	1	0	0	0	0	0	1	0	2
Death	0	0	0	1	0	1	0	0	2
Physician Decision	0	0	0	0	0	0	0	2	2
Study Terminated by Sponsor	0	0	0	0	0	0	1	0	1

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Baseline Characteristics

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg	Total
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	
Number of Participants [units: participants]	4	4	9	4	3	4	8	9	45
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation									
	56.0±8.83	52.3±4.50	64.8±10.34	58.0±13.29	48.0±17.44	57.3±16.32	48.6±15.56	58.1±14.23	56.3±13.35
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
Female	2	2	4	3	3	1	3	5	23
Male	2	2	5	1	0	3	5	4	22
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
Asian	1	1	3	1	0	1	1	2	10

White	3	3	6	3	3	3	7	7	35

Primary Outcome Result(s)

Number of participants with Dose-Limiting Toxicities (DLTs) in Cycle 1

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. Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher.

Time Frame: 28 days

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9

Number of participants with Dose-Limiting Toxicities (DLTs) (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)	Count of Participants (Percentage)
	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (12.5%)	0 (%)

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

Description: Number of participants with AEs and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. The on-treatment period is defined as the period from day of first dose of study medication to 30 days after last dose of study medication.

Time Frame: From first dose of study medication up to 30 days after last dose, with a maximum duration of 0.6 years for LHC165 single agent and 2.6 years for LHC165+PDR001

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Number of participants with Adverse Events (AEs) and Serious	**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)**	**Count of Participants (Percentage)**

Adverse Events (SAEs) during the on-treatment period (units: participants)								
AEs	3 (75%)	3 (75%)	7 (77.78%)	4 (100%)	3 (100%)	4 (100%)	7 (87.5%)	9 (100%)
Treatment-related AEs	2 (50%)	3 (75%)	5 (55.56%)	1 (25%)	0 (%)	4 (100%)	6 (75%)	7 (77.78%)
SAEs	1 (25%)	1 (25%)	1 (11.11%)	2 (50%)	0 (%)	1 (25%)	3 (37.5%)	1 (11.11%)
Treatment-related SAEs	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (12.5%)	0 (%)
Fatal SAEs	0 (%)	0 (%)	0 (%)	1 (25%)	0 (%)	1 (25%)	0 (%)	0 (%)
AEs leading to discontinuation	1 (25%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (12.5%)	0 (%)
Treatment-related AEs leading to discontinuation	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (12.5%)	0 (%)
AEs leading to dose adjustment/interruption	0 (%)	0 (%)	1 (11.11%)	1 (25%)	1 (33.33%)	1 (25%)	1 (12.5%)	0 (%)
AEs requiring additional therapy	2 (50%)	1 (25%)	6 (66.67%)	3 (75%)	1 (33.33%)	2 (50%)	6 (75%)	8 (88.89%)

Number of participants with dose reductions and dose interruptions of LHC165

Description: Number of participants with at least one dose reduction of LHC165 and number of participants with at least one dose interruption of LHC165.

Time Frame: From first dose of study medication up to last dose, with a maximum duration of 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**

Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Number of participants with dose reductions and dose interruptions of LHC165 (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)**	**Count of Participants (Percentage)**
At least 1 dose reduction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
At least 1 dose interruption	0 (%)	0 (%)	1 (11.11%)	0 (%)	0 (%)	1 (25%)	2 (25%)	1 (11.11%)

Dose intensity of LHC165

Description: Dose intensity of LHC165 was calculated as actual cumulative dose in micrograms divided by duration of exposure in days.

Time Frame: From first dose of study medication up to last dose, with a maximum duration of 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in	LHC165 200 µg bi-weekly in	LHC165 400 µg bi-weekly in	LHC165 600 µg bi-weekly in

					combination with PDR001 400 mg once every 4 weeks (Q4W)	combination with PDR001 400 mg once every 4 weeks (Q4W)	combination with PDR001 400 mg once every 4 weeks (Q4W)	combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Dose intensity of LHC165 (units: µg/day)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	7.140 (7.14 to 7.32)	14.290 (9.14 to 14.29)	28.570 (21.05 to 32.00)	42.860 (42.86 to 43.93)	7.140 (7.14 to 7.27)	12.410 (9.47 to 14.29)	28.570 (13.97 to 29.63)	40.000 (23.62 to 42.86)

Number of participants with dose reductions and dose interruptions of PDR001

Description: Number of participants with at least one dose reduction of PDR001 and number of participants with at least one dose interruption of PDR001. Dose reductions were not permitted for PDR001.

Time Frame: From first dose of study medication up to last dose, with a maximum duration of 2.5 years

	LHC165 100 µg Q2W + PDR001 400 mg	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	3	4	8	9
Number of participants with dose reductions and dose interruptions of PDR001 (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**

At least 1 dose reduction	0 (%)	0 (%)	0 (%)	0 (%)
At least 1 dose interruption	0 (%)	1 (25%)	1 (12.5%)	1 (11.11%)

Dose intensity of PDR001

Description: Dose intensity of PDR001 was calculated as actual cumulative dose in milligrams divided by duration of exposure in days.

Time Frame: From first dose of study medication up to last dose, with a maximum duration of 2.5 years

	LHC165 100 µg Q2W + PDR001 400 mg	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	3	4	8	9
Dose intensity of PDR001 (units: mg/day)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	14.290 (14.29 to 14.46)	14.365 (11.94 to 14.46)	14.290 (13.29 to 14.55)	14.180 (13.48 to 15.38)

Secondary Outcome Result(s)

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.

Time Frame From start of treatment until end of treatment, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
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)**	**Count of Participants (Percentage)**
Partial Response (PR)	0 (%)	1 (25%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (12.5%)	1 (11.11%)
Stable Disease (SD)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (50%)	0 (%)	3 (33.33%)
Progressive Disease (PD)	1 (25%)	3 (75%)	8 (88.89%)	2 (50%)	2 (66.67%)	2 (50%)	4 (50%)	5 (55.56%)
Unknown	3 (75%)	0 (%)	1 (11.11%)	2 (50%)	1 (33.33%)	0 (%)	3 (37.5%)	0 (%)

Overall Response Rate (ORR) per RECIST v1.1

Description Tumor response was based on local investigator assessment as per RECIST v1.1. ORR is defined as the percentage of participants with a best overall response of Complete Response (CR) or Partial Response (PR).

Time Frame From start of treatment until end of treatment, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Overall Response Rate (ORR) per RECIST v1.1 (units: percentage of participants)	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**
	0 (0.0 to 52.7)	25.0 (1.3 to 75.1)	0 (0.0 to 28.3)	0 (0.0 to 52.7)	0 (0.0 to 63.2)	0 (0.0 to 52.7)	12.5 (0.6 to 47.1)	11.1 (0.6 to 42.9)

Disease Control Rate (DCR) per RECIST v1.1

Description Tumor response was based on local investigator assessment as per RECIST v1.1. DCR is defined as the percentage of participants with a best overall response of Complete Response (CR), Partial Response (PR) or Stable Disease (SD).

Time Frame From start of treatment until end of treatment, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W +	LHC165 200 µg Q2W +	LHC165 400 µg Q2W +	LHC165 600 µg Q2W +

					PDR001 400 mg	PDR001 400 mg	PDR001 400 mg	PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Disease Control Rate (DCR) per RECIST v1.1 (units: percentage of participants)	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**
	0 (0.0 to 52.7)	25.0 (1.3 to 75.1)	0 (0.0 to 28.3)	0 (0.0 to 52.7)	0 (0.0 to 63.2)	50.0 (9.8 to 90.2)	12.5 (0.6 to 47.1)	44.4 (16.9 to 74.9)

Duration of Response (DOR) per RECIST v1.1

Description: DOR only applies to patients for whom best overall response is complete response (CR) or partial response (PR) based on local investigator assessment of overall lesion response according to RECIST v1.1. DOR is defined as the time from the date of first documented response (CR or PR) to the date of first documented progression or death due to study indication.

Time Frame: From first documented response to first documented progression or death due to study indication, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in	LHC165 200 µg bi-weekly in	LHC165 400 µg bi-weekly in	LHC165 600 µg bi-weekly in

					combination with PDR001 400 mg once every 4 weeks (Q4W)	combination with PDR001 400 mg once every 4 weeks (Q4W)	combination with PDR001 400 mg once every 4 weeks (Q4W)	combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	0	1	0	0	0	0	1	1
Duration of Response (DOR) per RECIST v1.1 (units: months)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
		3.81 (3.81 to 3.81)					29.70 (29.70 to 29.70)	13.77 (13.77 to 13.77)

Progression-Free Survival (PFS) per RECIST v1.1 (MTD/RDE only)

Description: PFS refers to the time from date of start of treatment to the date of event defined as the first documented progression or death due to any cause. If a patient had not had an event, PFS was censored at the date of last adequate tumor assessment. PFS was estimated using the Kaplan-Meier Method only if there were at least 5 patients within the same treatment group and the dose level was established as maximum tolerated dose (MTD)/recommended dose for expansion (RDE).

Time Frame: From start of treatment to first documented progression or death due to any cause, assessed up to 2.5 years

	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	9
Progression-Free Survival (PFS) per RECIST v1.1 (MTD/RDE only) (units: months)	**Number (90% Confidence Interval)**
	2.7 (1.7 to 3.6)

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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 immune-related RECIST (iRECIST).

Time Frame: From start of treatment until end of treatment, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
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)**	**Count of Participants (Percentage)**
iRECIST Partial Response (iPR)	0 (%)	1 (25%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (12.5%)	1 (11.11%)
iRECIST Stable Disease (iSD)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (50%)	1 (12.5%)	3 (33.33%)
iRECIST Confirmed Progressive Disease (iCPD)	0 (%)	0 (%)	0 (%)	0 (%)	1 (33.33%)	1 (25%)	0 (%)	3 (33.33%)
iRECIST Unconfirmed Progressive Disease (iUPD)	1 (25%)	3 (75%)	8 (88.89%)	2 (50%)	1 (33.33%)	1 (25%)	4 (50%)	2 (22.22%)

iUnknown	3 (75%)	0 (%)	1 (11.11%)	2 (50%)	1 (33.33%)	0 (%)	2 (25%)	0 (%)

Overall Response Rate (ORR) per iRECIST

Description: Tumor response was based on local investigator assessment as per iRECIST. ORR per iRECIST is defined as the percentage of participants with a best overall response of iRECIST complete response (iCR) or iRECIST partial response (iPR).

Time Frame: From start of treatment until end of treatment, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Overall Response Rate (ORR) per iRECIST (units: percentage of participants)	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**
	0 (0.0 to 52.7)	25.0 (1.3 to 75.1)	0 (0.0 to 28.3)	0 (0.0 to 52.7)	0 (0.0 to 63.2)	0 (0.0 to 52.7)	12.5 (0.6 to 47.1)	11.1 (0.6 to 42.9)

Disease Control Rate (DCR) per iRECIST

Description: Tumor response was based on local investigator assessment per iRECIST. DCR is defined as the percentage of participants with a best overall response of iRECIST complete response (iCR), iRECIST partial response (iPR) or iRECIST stable disease (iSD).

Time Frame: From start of treatment until end of treatment, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	4	3	4	8	9
Disease Control Rate (DCR) per iRECIST (units: percentage of participants)	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**
	0 (0.0 to 52.7)	25.0 (1.3 to 75.1)	0 (0.0 to 28.3)	0 (0.0 to 52.7)	0 (0.0 to 63.2)	50.0 (9.8 to 90.2)	25.0 (4.6 to 60.0)	44.4 (16.9 to 74.9)

Duration of Response (DOR) per iRECIST

Description: DOR only applies to patients for whom best overall response is iCR or iPR based on local investigator assessment of overall lesion response according to iRECIST. DOR is defined as the time from the date of first confirmed response (iCR or iPR) to the date of confirmed progression or death due to study indication.

Time Frame: From first confirmed response to first confirmed progression or death due to study indication, assessed up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	0	1	0	0	0	0	1	1
Duration of Response (DOR) per iRECIST (units: months)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
		3.81 (3.81 to 3.81)					29.70 (29.70 to 29.70)	13.77 (13.77 to 13.77)

Progression-Free Survival (PFS) per iRECIST (MTD/RDE only)

Description: PFS refers to the time from date of start of treatment to the date of event defined as the first documented confirmed progression or death due to any cause. If a patient had not had an event, PFS was censored at the date of last adequate tumor assessment. PFS was estimated using the Kaplan-Meier Method only if there were at least 5 patients within the same treatment group and the dose level was established as maximum tolerated dose (MTD)/recommended dose for expansion (RDE).

Time Frame: From start of treatment to first documented progression or death due to any cause, assessed up to 2.5 years

LHC165 600 µg Q2W + PDR001 400 mg

Arm/Group Description	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	9
Progression-Free Survival (PFS) per iRECIST (MTD/RDE only) (units: months)	**Number (90% Confidence Interval)**
	2.7 (1.7 to 3.6)

Maximum observed serum concentration (Cmax) of LHC165

Description: LHC165 was determined in serum by a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay. Pharmacokinetic (PK) parameters were calculated based on LHC165 serum concentrations by using non-compartmental methods.

Time Frame: pre-dose, 1, 2, 6, 24, 72 and 168 hours post-dose on Cycle 1 Day 1 (C1 D1) and Cycle 2 Day 15 (C2 D15). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	3	3	4	7	8
Maximum observed serum concentration	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**

(Cmax) of LHC165 (units: pg/mL)	**Coefficient of Variation)**	**Coefficient of Variation)**	**Coefficient of Variation)**	**Coefficient of Variation)**	**Coefficient of Variation)**	**Coefficient of Variation)**	**Coefficient of Variation)**	**Coefficient of Variation)**
C1 D1 (n=4,4,9,3,3,3,6,8)	1780 (45.4%)	2000 (153.2%)	3490 (165.8%)	2770 (41.8%)	281 (177.4%)	2330 (125.1%)	2960 (152.5%)	5010 (329.6%)
C2 D15 (n=0,3,2,0,1,3,3,8)		2340 (231.4%)	1410 (31.7%)		2780	3230 (238.0%)	2790 (193.5%)	8640 (166.2%)

Area under the serum concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LHC165

Description: LHC165 was determined in serum by a validated LC-MS/MS assay. PK parameters were calculated based on LHC165 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. The dosing interval (tau) was 14 days.

Time Frame: pre-dose, 1, 2, 6, 24, 72 and 168 hours post-dose on Cycle 1 Day 1 (C1 D1) and Cycle 2 Day 15 (C2 D15). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	4	4	9	3	3	4	7	8

Area under the serum concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LHC165 (units: h*pg/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)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1 D1 (n=4,4,9,3,1,3,5,6)	15000 (69.0%)	25800 (89.2%)	64500 (79.6%)	69400 (44.9%)	7140	37600 (20.5%)	45700 (53.9%)	136000 (96.1%)
C2 D15 (n=0,3,2,0,1,3,3,8)		20100 (260.4%)	29100 (110.3%)		23000	49600 (96.6%)	59400 (56.6%)	102000 (64.3%)

Area under the serum concentration-time curve from time zero to infinity (AUCinf) of LHC165

Description: LHC165 was determined in serum by a validated LC-MS/MS assay. PK parameters were calculated based on LHC165 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.

Time Frame: pre-dose, 1, 2, 6, 24, 72 and 168 hours post-dose on Cycle 1 Day 1 (C1 D1) and Cycle 2 Day 15 (C2 D15). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W	**LHC165 200 µg Q2W**	**LHC165 400 µg Q2W**	**LHC165 600 µg Q2W**	**LHC165 100 µg Q2W + PDR001 400 mg**	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)

					4 weeks (Q4W)			
Number of Participants Analyzed [units: participants]	4	4	9	3	3	4	7	8
Area under the serum concentration-time curve from time zero to infinity (AUCinf) of LHC165 (units: h*pg/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)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1 D1 (n=4,3,8,2,1,3,5,6)	15100 (71.4%)	33800 (63.8%)	71300 (75.7%)	68200 (71.6%)	6870	36600 (24.3%)	46100 (54.5%)	138000 (93.2%)
C2 D15 (n=0,3,2,0,0,3,3,7)		16100 (327.4%)	29000 (115.5%)			51400 (109.6%)	56400 (61.8%)	119000 (59.7%)

Maximum observed serum concentration (Cmax) of PDR001

Description: PDR001 was determined in serum by a validated LC-MS/MS assay. PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods.

Time Frame: pre-dose, 1, 24, 72, 168, 336 and 672 hours post-dose on Cycle 1 Day 1 (C1 D1) and pre-dose, 168, 336, 504 and 672 hours post-dose on Cycle 2 Day 1 (C2 D1). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W + PDR001 400 mg	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)

Number of Participants Analyzed [units: participants]	3	4	7	8
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)**
C1 D1 (n=3,4,7,8)	41.9 (36.1%)	82.5 (18.8%)	94.4 (28.5%)	99.1 (19.1%)
C2 D1 (n=1,3,3,8)	46	34.9 (67.9%)	53.3 (9.5%)	79.5 (24.2%)

Area under the serum concentration-time curve from time zero to the end of the dosing interval (AUCtau) of PDR001

Description: PDR001 was determined in serum by a validated LC-MS/MS assay. PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. The dosing interval (tau) was 28 days.

Time Frame: pre-dose, 1, 24, 72, 168, 336 and 672 hours post-dose on Cycle 1 Day 1 (C1 D1) and pre-dose, 168, 336, 504 and 672 hours post-dose on Cycle 2 Day 1 (C2 D1). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W + PDR001 400 mg	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	3	4	7	8
Area under the serum concentration-time curve from time zero to the end of the dosing interval (AUCtau) of PDR001 (units: h*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)**
C1 D1 (n=2,4,7,8)	15400 (111.4%)	18600 (12.9%)	18700 (36.5%)	32100 (14.7%)
C2 D1 (n=1,2,3,6)	24800	17400 (60.6%)	26600 (8.9%)	36600 (28.3%)

Area under the serum concentration-time curve from time zero to infinity (AUCinf) of PDR001

Description: PDR001 was determined in serum by a validated LC-MS/MS assay. PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.

Time Frame: pre-dose, 1, 24, 72, 168, 336 and 672 hours post-dose on Cycle 1 Day 1 (C1 D1) and pre-dose, 168, 336, 504 and 672 hours post-dose on Cycle 2 Day 1 (C2 D1). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W + PDR001 400 mg	**LHC165 200 µg Q2W + PDR001 400 mg**	**LHC165 400 µg Q2W + PDR001 400 mg**	**LHC165 600 µg Q2W + PDR001 400 mg**
Arm/Group Description	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	0	1	0	1
Area under the serum concentration-time curve from time zero to infinity (AUCinf) of PDR001 (units: h*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)**
C1 D1 (n=0,1,0,1)		21700		31600
C2 D1 (n=0,0,0,1)				26400

Number of participants with anti-drug antibodies (ADA) against PDR001

Description: Immunogenicity was evaluated in serum in a validated three-tiered assay approach. Samples were screened for potential anti-PDR001 antibodies and positive screen results were confirmed using a confirmatory assay. For confirmed ADA positive samples, titers were determined. 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

Time Frame: Baseline (before first dose) and post-baseline (assessed throughout the treatment up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001).

	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	1	3	6	9
Number of participants with anti-drug antibodies (ADA) against PDR001 (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
ADA-negative at baseline	1 (100%)	3 (100%)	6 (100%)	9 (100%)
ADA-positive at baseline	0 (%)	0 (%)	0 (%)	0 (%)
ADA-negative post-baseline	1 (100%)	2 (66.67%)	5 (83.33%)	8 (88.89%)
Treatment-induced ADA-positive	0 (%)	1 (33.33%)	1 (16.67%)	1 (11.11%)
Treatment-boosted ADA-positive	0 (%)	0 (%)	0 (%)	0 (%)

Percentage change from baseline of Tumor Infiltrating Lymphocytes (TILs) in injected lesions

Description: The expression of CD8 was measured in tumor samples (injected lesions) by immunohistochemical methods.

Time Frame: Baseline (screening), Cycle 2 Day 1 (C2 D1), Cycle 3 Day 1 (C3 D1) and end of treatment (up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001). The duration of each cycle was 28 days.

LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W +	LHC165 200 µg Q2W +	LHC165 400 µg Q2W +	LHC165 600 µg Q2W +

					PDR001 400 mg	PDR001 400 mg	PDR001 400 mg	PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	0	1	1	0	1	2	2	3
Percentage change from baseline of Tumor Infiltrating Lymphocytes (TILs) in injected lesions (units: percentage change of CD8 Permkar)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
C2 D1 (n=0,0,1,0,0,0,0,2)			2.630 (2.630 to 2.630)					-3.010 (-5.97 to -0.05)
C3 D1 (n=0,1,0,0,1,2,2,3)		5.340 (5.340 to 5.340)			-1.330 (-1.330 to -1.330)	1.445 (-1.46 to 4.35)	-0.195 (-0.28 to -0.11)	1.360 (-4.69 to 4.26)
End of Treatment (n=0,1,0,0,0,0,1,2)		0.030 (0.030 to 0.030)					-0.020 (-0.020 to -0.020)	-0.825 (-1.43 to -0.22)

Percentage change from baseline of Tumor Infiltrating Lymphocytes (TILs) in non-injected lesions

Description	The expression of CD8 was measured in tumor samples (non-injected lesions) by immunohistochemical methods.
Time Frame	Baseline (screening), Cycle 2 Day 1 (C2 D1), Cycle 3 Day 1 (C3 D1), Cycle 5 Day 1 (C5 D1) and end of treatment (up to 0.5 years for LHC165 single agent and 2.5 years for LHC165+PDR001). The duration of each cycle was 28 days.

	LHC165 100 µg Q2W	LHC165 200 µg Q2W	LHC165 400 µg Q2W	LHC165 600 µg Q2W	LHC165 100 µg Q2W + PDR001 400 mg	LHC165 200 µg Q2W + PDR001 400 mg	LHC165 400 µg Q2W + PDR001 400 mg	LHC165 600 µg Q2W + PDR001 400 mg
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)
Number of Participants Analyzed [units: participants]	0	1	3	0	0	2	2	3
Percentage change from baseline of Tumor Infiltrating Lymphocytes (TILs) in non-injected lesions (units: percentage change of CD8 Permkar)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
C2 D1 (n=0,0,3,0,0,0,0,3)			1.560 (0.63 to 6.21)					4.580 (-0.03 to 8.35)
C3 D1 (n=0,0,0,0,0,2,2,1)						3.200 (2.63 to 3.77)	2.070 (-0.15 to 4.29)	0.040 (0.04 to 0.04)
C5 D1 (n=0,0,0,0,0,0,0,1)								-1.930 (-1.930 to -1.930)
End of Treatment (n=0,1,0,0,0,0,1,2)		0.450 (0.450 to 0.450)					0.840 (0.840 to 0.840)	4.550 (-0.69 to 9.79)

Safety Results

Time Frame	From first dose of study medication up to 30 days after last dose (single agent arm) and up to 150 days after last dose (combination arm), with a maximum duration of 0.6 years for LHC165 single agent and 2.9 years for LHC165+PDR001.
Additional Description	Any sign or symptom that occurs during the study treatment plus 30 days after last dose (single agent arm) and plus 150 days after last dose (combination arm).
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	LHC165 100 µg Q2W N = 4	**LHC165 200 µg Q2W N = 4**	**LHC165 400 µg Q2W N = 9**	**LHC165 600 µg Q2W N = 4**	**All LHC165 Q2W N = 21**	**LHC165 100 µg Q2W + PDR001 400 mg N = 3**	**LHC165 200 µg Q2W + PDR001 400 mg N = 4**	**LHC165 400 µg Q2W + PDR001 400 mg N = 8**	**LHC165 600 µg Q2W + PDR001 400 mg N = 9**	**All LHC165 + PDR001 N = 24**	**All Participants N = 45**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	All participants treated with LHC165 single agent	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	All participants treated with LHC165 in combination with PDR001	All participants in the trial

Total Number Affected	0	0	2	1	3	0	2	1	1	4	7
Total Number At Risk	4	4	9	4	21	3	4	8	9	24	45

Serious Adverse Events

	LHC165 100 µg Q2W N = 4	**LHC165 200 µg Q2W N = 4**	**LHC165 400 µg Q2W N = 9**	**LHC165 600 µg Q2W N = 4**	**All LHC165 Q2W N = 21**	**LHC165 100 µg Q2W + PDR001 400 mg N = 3**	**LHC165 200 µg Q2W + PDR001 400 mg N = 4**	**LHC165 400 µg Q2W + PDR001 400 mg N = 8**	**LHC165 600 µg Q2W + PDR001 400 mg N = 9**	**All LHC165 + PDR001 N = 24**	**All Participants N = 45**
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	All participants treated with LHC165 single agent	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	All participants treated with LHC165 in combination with PDR001	All participants in the trial
Total # Affected by any Serious Adverse Event	1	1	1	2	5	0	1	3	1	5	10
Total # at Risk by any Serious Adverse Event	4	4	9	4	21	3	4	8	9	24	45

Blood and lymphatic system disorders											
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Leukocytosis	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Gastrointestinal disorders											
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Pancreatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Infections and infestations											
Bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Septic shock	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Injury, poisoning and procedural complications											
Tendon rupture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Metabolism and nutrition disorders											
Hyponatraemia	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)											
Tumour associated fever	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Respiratory, thoracic and mediastinal disorders											
Respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Skin and subcutaneous tissue disorders											
Skin ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Vascular disorders											
Hypotension	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 5%

	LHC165 100 µg Q2W N = 4	**LHC165 200 µg Q2W N = 4**	**LHC165 400 µg Q2W N = 9**	**LHC165 600 µg Q2W N = 4**	**All LHC165 Q2W N = 21**	**LHC165 100 µg Q2W + PDR001**	**LHC165 200 µg Q2W + PDR001**	**LHC165 400 µg Q2W + PDR001**	**LHC165 600 µg Q2W + PDR001**	**All LHC165 +**	**All Participants N = 45**

						400 mg N = 3	400 mg N = 4	400 mg N = 8	400 mg N = 9	PDR001 N = 24	
Arm/Group Description	LHC165 100 µg bi-weekly	LHC165 200 µg bi-weekly	LHC165 400 µg bi-weekly	LHC165 600 µg bi-weekly	All participants treated with LHC165 single agent	LHC165 100 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 200 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 400 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	LHC165 600 µg bi-weekly in combination with PDR001 400 mg once every 4 weeks (Q4W)	All participants treated with LHC165 in combination with PDR001	All participants in the trial
Total # Affected by any Other Adverse Event	3	3	7	4	17	3	4	7	9	23	40
Total # at Risk by any Other Adverse Event	4	4	9	4	21	3	4	8	9	24	45
Blood and lymphatic system disorders											
Anaemia	0 (0.00%)	1 (25.00%)	1 (11.11%)	3 (75.00%)	5 (23.81%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	4 (44.44%)	6 (25.00%)	11 (24.44%)
Leukocytosis	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (25.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Leukopenia	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Lymphopenia	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	2 (4.44%)
Neutropenia	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Endocrine disorders											
Glucocorticoid deficiency	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)

Eye disorders											
Dry eye	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Lacrimation increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	2 (4.44%)
Visual acuity reduced	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Gastrointestinal disorders											
Abdominal distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	1 (11.11%)	3 (12.50%)	3 (6.67%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (4.76%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	3 (6.67%)
Anal pruritus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Cheilitis	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Constipation	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Dental caries	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Diarrhoea	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	2 (8.33%)	3 (6.67%)
Duodenal ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Dyspepsia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)

Dysphagia	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Flatulence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (4.76%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	2 (4.44%)
Lip pain	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (4.76%)	1 (33.33%)	1 (25.00%)	1 (12.50%)	2 (22.22%)	5 (20.83%)	6 (13.33%)
Odynophagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Oral cavity fistula	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Pancreatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Stomatitis	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Vomiting	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (25.00%)	2 (9.52%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	2 (22.22%)	4 (16.67%)	6 (13.33%)
General disorders and administration site conditions											
Asthenia	0 (0.00%)	1 (25.00%)	1 (11.11%)	3 (75.00%)	5 (23.81%)	0 (0.00%)	1 (25.00%)	2 (25.00%)	0 (0.00%)	3 (12.50%)	8 (17.78%)
Axillary pain	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	2 (4.44%)
Chills	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	2 (25.00%)	2 (22.22%)	4 (16.67%)	5 (11.11%)
Face oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)

Fatigue	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	2 (9.52%)	1 (33.33%)	0 (0.00%)	1 (12.50%)	1 (11.11%)	3 (12.50%)	5 (11.11%)
Influenza like illness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Infusion site extravasation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Injection site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Injection site reaction	1 (25.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	3 (14.29%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	5 (11.11%)
Malaise	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	1 (11.11%)	2 (8.33%)	2 (4.44%)
Mucosal inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	4 (8.89%)
Pain	1 (25.00%)	1 (25.00%)	0 (0.00%)	1 (25.00%)	3 (14.29%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	4 (8.89%)
Pyrexia	0 (0.00%)	1 (25.00%)	5 (55.56%)	0 (0.00%)	6 (28.57%)	0 (0.00%)	2 (50.00%)	5 (62.50%)	4 (44.44%)	11 (45.83%)	17 (37.78%)
Hepatobiliary disorders											
Hypertransaminasaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Immune system disorders											
Cytokine release syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Infections and infestations											

Infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Pulpitis dental	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Suspected COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Upper respiratory tract infection	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Wound infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Injury, poisoning and procedural complications											
Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Lip injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Vaccination complication	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Investigations											
Activated partial thromboplastin time prolonged	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Alanine aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (8.33%)	2 (4.44%)

Blood alkaline phosphatase increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Blood lactate dehydrogenase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Blood phosphorus increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Blood thyroid stimulating hormone increased	1 (25.00%)	1 (25.00%)	0 (0.00%)	1 (25.00%)	3 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.67%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	2 (4.44%)
Lipase increased	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (25.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Platelet count increased	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
SARS-CoV-2 test negative	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Metabolism and nutrition disorders											
Decreased appetite	0 (0.00%)	0 (0.00%)	2 (22.22%)	1 (25.00%)	3 (14.29%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	0 (0.00%)	2 (8.33%)	5 (11.11%)
Hyperamylasaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Hypercalcaemia	1 (25.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)

Hyperglycaemia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	2 (4.44%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Hyperlipasaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Hypocalcaemia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Hypoglycaemia	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Hypokalaemia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Hyponatraemia	1 (25.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	3 (14.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.67%)
Hypophosphataemia	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Musculoskeletal and connective tissue disorders											
Back pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	2 (4.44%)
Groin pain	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Mobility decreased	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Muscle spasms	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (8.33%)	2 (4.44%)

Musculoskeletal pain	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Myalgia	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (25.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)											
Cancer pain	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Paraneoplastic syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Tumour associated fever	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Nervous system disorders											
Amnesia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	2 (8.33%)	2 (4.44%)
Dysgeusia	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	2 (4.44%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	1 (11.11%)	2 (8.33%)	2 (4.44%)
Vagus nerve disorder	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Psychiatric disorders											
Confusional state	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)

Hallucination	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Insomnia	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Renal and urinary disorders											
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	2 (8.33%)	2 (4.44%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Urine odour abnormal	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Reproductive system and breast disorders											
Breast inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Perineal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Prostatic obstruction	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Respiratory, thoracic and mediastinal disorders											
Catarrh	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Choking	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	2 (8.33%)	2 (4.44%)
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (25.00%)	2 (9.52%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	0 (0.00%)	2 (8.33%)	4 (8.89%)

Increased viscosity of upper respiratory secretion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Nasal congestion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Productive cough	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	2 (4.44%)
Skin and subcutaneous tissue disorders											
Blister	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Dry skin	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.44%)
Lichenoid keratosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Night sweats	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)
Panniculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Pruritus	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	2 (50.00%)	1 (12.50%)	3 (33.33%)	6 (25.00%)	7 (15.56%)
Rash papular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (4.17%)	1 (2.22%)
Skin lesion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	1 (2.22%)
Vitiligo	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	0 (0.00%)	2 (8.33%)	2 (4.44%)
Vascular disorders											
Hypertension	2 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (9.52%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (4.17%)	3 (6.67%)

Hypotension	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (4.76%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.22%)

Conclusion:

- RDE was established as LHC165 600 µg biweekly in combination with PDR001 400 mg Q4W.
- In single agent arm, no DLT was observed. In combination arm, one DLT of pancreatitis was reported.
- Comparable exposures of LHC165 were observed at same dose levels in single agent and combination arms. There was no impact on PK of LHC165 when given in combination with PDR001.
- The safety profile of LHC165 was well characterized in all treatment groups evaluated in this study. No major differences were observed between LHC165 as single agent vs. LHC165 + PDR001 combination. Overall, the safety profile of the doses explored was generally manageable.

Date of Clinical Trial Report

28-Feb-2023