NOVARTIS

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

LGK974 (also known as WNT974) and spartalizumab (PDR001)

Trial Indication(s)

- Melanoma, lung squamous cell cancer (SCC), or head and neck SCC (HNSCC) that was primary refractory to prior anti-PD-1 treatment.
- Esophageal SCC, cervical SCC, or triple negative breast cancer (TNBC)

Protocol Number

CLGK974X2101

Protocol Title

A Phase I, open-label, dose escalation study of oral LGK974 in patients with malignancies dependent on Wnt ligands

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1 (LGK974) and Phase 3 (PDR001)

NOVARTIS

Study Start/End Dates

Study Start Date: December 01, 2011 (Actual)
Primary Completion Date: June 01, 2021 (Actual)
Study Completion Date: June 17, 2024 (Actual)

Study Design/Methodology

This open-label, multicenter, phase 1 dose escalation study was the first to administer LGK974 to humans. The study comprised of two portions: a dose escalation of LGK974 as a single agent, followed by a safety expansion in specific disease indications; and a dose escalation of LGK974 in combination with PDR001, followed by a safety expansion in cutaneous melanoma.

Dose escalation and expansion for LGK974 as a single agent

Patients were administered LGK974 for a 28-day cycle according to their assigned dosing schedule (i.e. once daily (QD), twice daily (BID), intermittent dosing). The dose escalation was continued until the maximum tolerated dose (MTD)/recommended dose for expansion (RDE) was reached. A Bayesian logistic regression model (BLRM) employing the escalation with overdose control (EWOC) was used during the escalation part for dose level selection and for determination of the MTD. At the end of the dose escalation part, a dose at or lower than the MTD of LGK974 was selected for further evaluation based on an overall clinical assessment of all available safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) data. Measurable disease was required for patients enrolled in the expansion part.

Dose escalation and expansion for LGK974 in combination with PDR001

This portion of the study was designed to evaluate the safety, tolerability, PK, PD, and preliminary anti-tumor activity of LGK974 in combination with PDR001 and had a dose escalation and dose expansion part. Several schedules of LGK974 dosing were explored (i.e. LGK974 QD dosing on Day 1 through 8 of Cycle 1 only; LGK974 QD dosing on Day 1 through 15 of Cycle 1 only; or Cycle 1-4 LGK974 QD dosing on Day 1 through 8 each cycle), and the dose escalation was continued until the MTD and/or RDE was reached.

The expansion part of the study was initiated at the determination of the RDE and was carried out with one regimen. The goal of the expansion part was to better characterize the safety and tolerability, PK/PD relationship as well as to explore the anti-tumor activity of the combination.

Centers

20 centers in 7 countries: United States(6), Netherlands(2), Spain(7), Italy(2), France(1), Canada(1), Germany(1)

Objectives:

The primary objective of the trial was to determine the MTD and/or RDE of LGK974 as a single agent and in combination with PDR001 when administered to adult patients with malignancies as specified in the inclusion criteria.

The secondary objectives were:

- Characterize the safety and tolerability of LGK974 as a single agent and in combination with PDR001
- Evaluate the single dose and multiple dose PK of LGK974 and its pharmacologically active metabolite, LHA333, following single agent LGK974 dosing, and PK of LGK974, LHA333 and PDR001 when LGK974 and PDR001 are dosed in combination
- Assess the PD response to LGK974 in tumor tissue and/or skin
- Establish the PK/PD relationship of LGK974
- Assess the anti-tumor activity of LGK974
- Assess the anti-tumor activity LGK974 in combination with PDR001

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

In the single agent part, study drug and study treatment both referred to LGK974 and were used interchangeably. In the combination part, study drug referred to the individual compound i.e., LGK974 or PDR001. Study treatment referred to combination of LGK974 and PDR001.

Dosing regimen of LGK974 as a single agent

LGK974 was administered orally as capsules in 28-day cycles. The following treatment schedules were assessed:

- Once daily (QD) continuous dosing at dose levels ranging from 5 to 30 mg.
- Twice daily (BID) continuous dosing at a dose of 5 mg.
- Intermittent dosing, 4 days of dosing followed by 3-day break, at doses of 30 and 45 mg.

Dosing regimen of LGK974 in combination with PDR001

PDR001 in combination with LGK974 was administered in 28-day cycles.

PDR001 400 mg was administered as intravenous infusion on Day 1 of every cycle (Q4W) and was not escalated.

LGK974 was given orally as capsules and administered intermittently when combined with PDR001. The following treatment schedules were assessed:

- QD dosing on Days 1 through 8 of Cycle 1 only, at doses of 2.5, 5 and 10 mg.
- QD dosing on Days 1 through 15 of Cycle 1 only, at a dose of 2.5 mg.
- QD dosing on Days 1 through 8 of each Cycle 1 to 4, at doses of 2.5, 5 and 10 mg.

Patients were treated until disease progression, unacceptable toxicity, or withdrawal of consent.

Statistical Methods

Primary endpoint: The corresponding primary analysis was based on an adaptive BLRM guided by the EWOC principle using the methodology. The MTD was evaluated for preliminary efficacy and overall tolerability during the dose expansion part of the trial. The primary variable is the frequency of dose-limiting toxicities (DLTs) associated with continuous daily administration of LGK974 during the first cycle of the treatment or LGK974 in combination with PDR001 during the first 2 cycles of study treatment.

Secondary endpoints: The secondary endpoints were as below.

Efficacy: In terms of Overall Response Rate (ORR) which comprised of Complete Response (CR) and Partial Response (PR), as assessed by RECIST v1.1 and/or irRC (only in the combination study portion), and Duration of Response (DOR) for all responders.

Safety: All tables were presented by treatment group (dose level per dosing schedule), with participants classified to dose groups.

Pharmacokinetics: Descriptive statistics were used to assess the PK endpoints.

Pharmacodynamic: Measured by post-treatment change from baseline in AXIN2 geneexpression levels.

Pharmacokinetics/Pharmacodynamic: The post-treatment change or log fold change from baseline in AXIN2 mRNA were regressed onto PK parameters at steady state using an appropriate statistical model

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Diagnosis of locally advanced or metastatic cancer that has progressed despite standard therapy or for which no effective standard therapy exists and histological confirmation of one of the following diseases indicated below:

- Single Agent Dose escalation part: documented B-RAF mutant colorectal cancer or pancreatic adenocarcinoma. In

addition, tumors of any histological origin with documented genetic alterations upstream in the Wnt signaling pathway were eligible with prior agreement with Novartis.

- Single Agent Dose expansion part: documented B-RAF mutant colorectal cancer with documented RNF43 mutation and/or RSPO fusion or pancreatic adenocarcinoma with documented RNF43 mutation. In addition, patients with tumors of any histological origin with documented genetic alterations upstream in the Wnt signaling pathway (e.g. RNF43 or RSPO fusion) were eligible with prior agreement with Novartis

- LGK974 with PDR001: Dose escalation: patients with the following cancers that were previously treated with anti-PD-1 therapy and whose best response on that therapy was progressive disease (i.e. primary refractory): melanoma, lung SCC, HNSCC. Patients with esophageal SCC, cervical SCC or TNBC who are either naïve or primary refractory to prior anti-PD-1 therapy.
- LGK974 with PDR001: Dose expansion: patients with:
• cutaneous melanoma that was primary refractory to prior anti-PD-1 therapy, defined as a best response of progressive disease or stable disease for <= 4 months, or disease recurrence with the first 6 months of adjuvant therapy. Patients with BRAF V600-mutant melanoma must have also received and been failed by prior systemic therapy with BRAF V600 inhibitor, with or without a MEK inhibitor.
• Cutaneous melanoma with acquired resistance to prior anti-PD-1 therapy, defined as progressive disease following response (PR or CR) or following stable disease for > 4 months. Patients with BRAF V600-mutant melanoma must have also received and been failed by prior systemic therapy with a BRAF V600 inhibitor, with or without a MEK inhibitor.

Exclusion Criteria:

- Impaired cardiac function
- Impairment of gastrointestinal function or gastrointestinal disease that may significantly alter the absorption of LGK974 (e.g., ulcerative diseases, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, small bowel resection)
- Brain metastases that have not been adequately treated
- Malignant disease other than that being treated in this study
- Laboratory abnormalities as specified in the protocol
- Osteoporosis, osteopenia
- Bone fractures within the past year
- Pathologic bone fracture
- Active, known or suspected autoimmune disease or severe hypersensitivity reactions to other monoclonal antibodies

NOVARTIS

Participant Flow Table

LGK974 single agent

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID	LGK974 10mg QD pancreatic adenocarcinoma	LGK974 10mg QD colorectal	LGK974 10mg QD Any
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID	Expansion part: LGK974 10 mg QD in pancreatic adenocarcinoma	Expansion part: LGK974 10 mg QD in colorectal cancer	Expansion part: LGK974 10 mg QD in tumor types of any histological origin with documented genetic alterations that modify upstream Wnt signaling
Started	6	6	10	11	10	6	5	4	3	5	7	9	12
Completed	0	0	0	0	0	0	0	0	0	0	0	0	0
Not Completed*	6	6	10	11	10	6	5	4	3	5	7	9	12
Adverse Event	0	0	2	1	2	1	2	0	0	0	0	2	2

Subject withdrew consent	1	2	0	1	1	0	0	2	0	0	0	0	1
Death	1	0	0	0	0	0	0	0	1	0	0	0	0
Disease progression	4	4	8	9	7	5	3	2	2	5	7	7	8
Administrative problems	0	0	0	0	0	0	0	0	0	0	0	0	1

* Not completed refers to treatment discontinuation. The reasons for discontinuation are listed below.

Combination treatment LGK974+PDR001, and Total in the study

	LGK974 2.5mg QD C1 D1-8 + PDR001	**LGK974 5mg QD C1 D1-8 + PDR001**	**LGK974 10mg QD C1 D1-8 + PDR001**	**LGK974 2.5mg QD C1 D1-15 + PDR001**	**LGK974 2.5mg QD C1-4 D1-8 + PDR001**	**LGK974 5mg QD C1-4 D1-8 + PDR001**	**LGK974 10mg QD C1-4 D1-8 + PDR001**	**LGK974 10mg QD C1-4 D1-8 + PDR001 PrR**	**LGK974 10mg QD C1-4 D1-8 + PDR001 AR**	**Total**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma that was primary refractory to prior	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma with acquired resistance to prior	All patients in the study

								anti-PD-1 therapy	anti-PD-1 therapy	
Started	5	4	4	11	5	14	8	25	15	185
Completed	0	0	0	0	0	0	0	0	0	0
Not Completed*	5	4	4	11	5	14	8	25	15	185
Adverse Event	0	0	0	1	2	1	0	1	1	18
Subject withdrew consent	2	1	1	1	0	0	0	0	0	13
Death	0	0	0	1	0	1	1	1	0	6
Disease progression	3	3	3	8	3	12	6	18	14	141
Administrative problems	0	0	0	0	0	0	1	5	0	7

* Not completed refers to treatment discontinuation. The reasons for discontinuation are listed below.

Baseline Characteristics

LGK974 single agent

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**	**LGK974 10mg QD pancreatic adenocarcinoma**	**LGK974 10mg QD colorectal**	**LGK974 10mg QD Any**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of	Escalation part: LGK974 45 mg QD, 4 days of	Escalation part: LGK974 5 mg BID	Expansion part: LGK974 10 mg QD in pancreatic	Expansion part: LGK974 10 mg QD in	Expansion part: LGK974 10 mg QD in tumor

								dosing followed by 3-day break	dosing followed by 3-day break		adenocarcinoma	colorectal cancer	types of any histological origin with documented genetic alterations that modify upstream Wnt signaling
Number of Participants [units: participants]	6	6	10	11	10	6	5	4	3	5	7	9	12
Baseline Analysis Population Description													
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation													
	50.7±9.91	50.5±15.00	59.6±10.27	55.5±12.75	55.5±9.62	61.5±5.39	65.2±8.76	54.5±20.09	58.0±13.11	62.2±6.46	61.6±8.83	55.0±7.50	60.1±10.81
Age, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													

18 - <65 years	6	5	6	8	9	4	3	2	2	3	4	8	8
65 - <85 years	0	1	4	3	1	2	2	2	1	2	3	1	4
>=85 years	0	0	0	0	0	0	0	0	0	0	0	0	0
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													
Female	4	4	4	6	8	3	2	3	2	1	5	4	8
Male	2	2	6	5	2	3	3	1	1	4	2	5	4
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													
Caucas ian	5	4	9	9	9	6	4	3	3	4	6	9	12
Black	1	1	0	0	1	0	0	1	0	1	0	0	0
Asian	0	0	0	1	0	0	0	0	0	0	0	0	0
Pacific Islander	0	0	0	0	0	0	0	0	0	0	1	0	0
Other	0	1	1	1	0	0	1	0	0	0	0	0	0
Missing	0	0	0	0	0	0	0	0	0	0	0	0	0

Combination treatment LGK974+PDR001, and Total in the study

	LGK974 2.5mg QD C1 D1-8 + PDR001	LGK974 5mg QD C1 D1-8 + PDR001	LGK974 10mg QD C1 D1-8 + PDR001	LGK974 2.5mg QD C1 D1-15 + PDR001	LGK974 2.5mg QD C1-4 D1-8 + PDR001	LGK974 5mg QD C1-4 D1-8 + PDR001	LGK974 10mg QD C1-4 D1-8 + PDR001	LGK974 10mg QD C1-4 D1-8	LGK974 10mg QD C1-4 D1-8	Total

								+ PDR001 PrR	+ PDR001 AR	
Arm/Group Description	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma that was primary refractory to prior anti-PD-1 therapy	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma with acquired resistance to prior anti-PD-1 therapy	All patients in the study
Number of Participants [units: participants]	5	4	4	11	5	14	8	25	15	185
Baseline Analysis Population Description										
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation										
	59.0±15.12	66.0±7.62	66.0±10.65	49.5±12.50	63.2±16.19	59.7±10.65	55.6±16.97	57.1±13.95	62.7±12.01	58.09±12.117

Age, Customized
(units: participants)
Analysis Population Type: Participants
Count of Participants (Not Applicable)

18 - <65 years	4	2	1	9	2	8	4	19	8	125
65 - <85 years	1	2	3	2	3	6	4	6	7	60
>=85 years	0	0	0	0	0	0	0	0	0	0

Sex: Female, Male
(units: participants)
Analysis Population Type: Participants
Count of Participants (Not Applicable)

Female	2	1	2	9	3	8	5	6	7	97
Male	3	3	2	2	2	6	3	19	8	88

Race/Ethnicity, Customized
(units: participants)
Analysis Population Type: Participants
Count of Participants (Not Applicable)

Caucasian	5	3	2	6	5	9	5	24	14	156
Black	0	1	1	2	0	0	0	0	0	9
Asian	0	0	1	0	0	1	0	0	0	3
Pacific Islander	0	0	0	0	0	0	0	0	0	1
Other	0	0	0	3	0	4	3	0	0	14
Missing	0	0	0	0	0	0	0	1	1	2

NOVARTIS

Primary Outcome Result(s)

Number of participants with Dose-Limiting Toxicities (DLTs) in the Dose Escalation

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, intercurrent illness or concomitant medications, which occurs within the first cycle (28 days) of treatment with LGK974 as single agent or in the first two cycles (56 days) of treatment when LGK974 is given in combination with PDR001 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.
Time Frame	28 days (LGK974 single agent) and 56 days (LGK974+PDR001)
Analysis Population Description	Patients in the dose escalation part who either met the minimum exposure criterion defined in the protocol and had sufficient safety evaluations, or had experienced a DLT during Cycle 1 (LGK974 single agent) or during the first 2 cycles (LGK974+PDR001).

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5 mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**	**LGK974 2.5mg QD C1 D1-8 + PDR001**	**LGK974 5mg QD C1 D1-8 + PDR001**	**LGK974 10mg QD C1 D1-8 + PDR001**	**LGK974 2.5mg QD C1 D1-15 + PDR001**	**LGK974 2.5mg QD C1-4 D1-8 + PDR001**	**LGK974 5mg QD C1-4 D1-8 + PDR001**	**LGK974 10mg QD C1-4 D1-8 + PDR001**
Arm/ Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of Cycle	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of Cycle	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of Cycle	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 15 of Cycle	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of each	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of each	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of each

											1 only and PDR001 400 mg Q4W	1 only and PDR001 400 mg Q4W	1 only and PDR001 400 mg Q4W	1 only and PDR001 400 mg Q4W	Cycle 1 to 4 and PDR001 400 mg Q4W	Cycle 1 to 4 and PDR001 400 mg Q4W	Cycle 1 to 4 and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	4	4	6	7	5	4	3	2	2	4	5	4	4	11	4	11	5
Number of participants with Dose-Limiting Toxicities (DLTs) in the Dose Escalation (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)**	**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)**	**Count of Participants (Percentage)**

At least one DLT	0 (%)	0 (%)	2 (33.33 %)	1 (14.29 %)	0 (%)	1 (25%)	1 (33.33 %)	0 (%)	0 (%)	1 (25%)	0 (%)	0 (%)	0 (%)	1 (9.09 %)	1 (25%)	0 (%)	0 (%)
Constipation	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (25%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Asthenia	0 (%)	0 (%)	1 (16.67 %)	1 (14.29 %)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Fatigue	0 (%)	0 (%)	1 (16.67 %)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Dysgeusia	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (33.33 %)	0 (%)	0 (%)	1 (25%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Epilepsy	0 (%)	0 (%)	1 (16.67 %)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Spinal compression fracture	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (25%)	0 (%)	0 (%)
Arthralgia	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (9.09 %)	0 (%)	0 (%)	0 (%)

NOVARTIS

Secondary 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 and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. AE grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. For CTCAE v4.03, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life-threatening; Grade 5 = death related to AE. 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 medication up to 30 days after last dose, with a maximum duration of 0.6 years for LGK974 and 3.6 years for LGK974+PDR001
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation or in the dose expansion. Patients were analyzed according to the study treatment received.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+ Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5 mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**	**LGK974 2.5mg QD C1 D1-8 + PDR001**	**LGK974 5mg QD C1 D1-8 + PDR001**	**LGK974 10mg QD C1 D1-8 + PDR001**	**LGK974 2.5mg QD C1 D1-15 + PDR001**	**LGK974 2.5mg QD C1-4 D1-8 + PDR001**	**LGK974 5mg QD C1-4 D1-8 + PDR001**	**LGK974 10mg QD C1-4 D1-8 + PDR001 Esc+ Exp**
Arm/ Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing follow	Escalation part: LGK974 45 mg QD, 4 days of dosing	Escalation part: LGK974 5 mg BID	Escalation part: LGK974 2.5 mg QD dosing on Days 1	Escalation part: LGK974 5 mg QD dosing on Days 1	Escalation part: LGK974 10 mg QD dosing on Days 1	Escalation part: LGK974 2.5 mg QD dosing on Days 1	Escalation part: LGK974 2.5 mg QD dosing on Days 1	Escalation part: LGK974 5 mg QD dosing on Days 1	Escalation and expansion: LGK974 10 mg QD dosing on

								ed by 3-day break	follow ed by 3-day break		throu gh 8 of Cycle 1 only and PDR0 01 400 mg Q4W	throu gh 8 of Cycle 1 only and PDR0 01 400 mg Q4W	throu gh 8 of Cycle 1 only and PDR0 01 400 mg Q4W	throu gh 15 of Cycle 1 only and PDR0 01 400 mg Q4W	throu gh 8 of each Cycle 1 to 4 and PDR0 01 400 mg Q4W	throu gh 8 of each Cycle 1 to 4 and PDR0 01 400 mg Q4W	Days 1 throu gh 8 of each Cycle 1 to 4 and PDR0 01 400 mg Q4W
Numb er of Partic ipant s Analy zed [units : partic ipant s]	6	6	38	11	10	6	5	4	3	5	5	4	4	11	5	14	48
Numb er of partic ipant s with Adver se Event s (AEs) and Serio us Adver se	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**	**Coun t of Partic ipant s (Not Appli cable)**

Events (SAEs) during the on-treatment period (units: participants)																	
AEs	6 (100%)	6 (100%)	38 (100%)	11 (100%)	10 (100%)	6 (100%)	5 (100%)	4 (100%)	3 (100%)	5 (100%)	5 (100%)	4 (100%)	4 (100%)	11 (100%)	5 (100%)	14 (100%)	48 (100%)
Treatment-related AEs	2 (33.33%)	4 (66.67%)	34 (89.47%)	9 (81.82%)	9 (90%)	4 (66.67%)	3 (60%)	4 (100%)	2 (66.67%)	4 (80%)	5 (100%)	2 (50%)	3 (75%)	8 (72.73%)	4 (80%)	13 (92.86%)	38 (79.17%)
AEs with grade ≥ 3	3 (50%)	5 (83.33%)	26 (68.42%)	8 (72.73%)	9 (90%)	5 (83.33%)	4 (80%)	1 (25%)	3 (100%)	2 (40%)	2 (40%)	3 (75%)	2 (50%)	4 (36.36%)	4 (80%)	8 (57.14%)	18 (37.5%)
Treatment-related AEs with grade ≥ 3	0 (%)	1 (16.67%)	12 (31.58%)	3 (27.27%)	3 (30%)	4 (66.67%)	1 (20%)	0 (%)	1 (33.33%)	0 (%)	0 (%)	1 (25%)	1 (25%)	1 (9.09%)	0 (%)	2 (14.29%)	6 (12.5%)
SAEs	3 (50%)	4 (66.67%)	22 (57.89%)	5 (45.45%)	7 (70%)	4 (66.67%)	4 (80%)	2 (50%)	3 (100%)	1 (20%)	3 (60%)	3 (75%)	1 (25%)	2 (18.18%)	4 (80%)	7 (50%)	12 (25%)
Treatment-relate	0 (%)	0 (%)	7 (18.42%)	1 (9.09%)	2 (20%)	3 (50%)	0 (%)	0 (%)	1 (33.33%)	1 (20%)	0 (%)	1 (25%)	0 (%)	0 (%)	2 (40%)	1 (7.14%)	1 (2.08%)

d
SAEs

Overall Response Rate (ORR) per RECIST v1.1

Description	Tumor response was based on local investigator assessment as per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1. ORR per RECIST v1.1 is defined as the percentage of participants with a best overall response of Complete Response (CR) or Partial Response (PR). For RECIST v1.1, CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to 0.5 years for LGK974 and 3.5 years for LGK974+PDR001
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation or in the dose expansion.

	LGK 974 5mg QD	**LGK 974 7.5 mg QD**	**LGK 974 10mg QD**	**LGK 974 15mg QD**	**LGK 974 20mg QD**	**LGK 974 22.5 mg QD**	**LGK 974 30mg QD**	**LGK 974 30mg 4/7 QD**	**LGK 974 45mg 4/7 QD**	**LGK 974 5mg BID**	**LGK 974 10mg QD Exp**	**LGK 974 2.5 mg QD C1 D1-8 + PDR 001**	**LGK 974 5mg QD C1 D1-8 + PDR 001**	**LGK 974 10mg QD C1 D1-8 + PDR 001**	**LGK 974 2.5 mg QD C1 D1-15 + PDR 001**	**LGK 974 2.5 mg QD C1-4 D1-8 + PDR 001**	**LGK 974 5mg QD C1-4 D1-8 + PDR 001**	**LGK 974 10mg QD C1-4 D1-8 + PDR 001**	**LGK 974 10mg QD C1-4 D1-8 + PDR 001 PrR**	**LGK 974 10mg QD C1-4 D1-8 + PDR 001 AR**
Arm/ Group Description	Escalation part: LGK 974 5 mg QD	Escalation part: LGK 974 5 mg QD	Escalation part: LGK 974 10 mg QD	Escalation part: LGK 974 15 mg QD	Escalation part: LGK 974 20 mg QD	Escalation part: LGK 974 22.5 mg QD	Escalation part: LGK 974 30 mg QD	Escalation part: LGK 974 30 mg, 4 days of	Escalation part: LGK 974 45 mg QD, 4 days	Escalation part: LGK 974 5 mg BID	Expansion part: LGK 974 10 mg QD	Escalation part: LGK 974 2.5 mg QD dosing	Escalation part: LGK 974 5 mg QD dosing	Escalation part: LGK 974 10 mg QD dosing	Escalation part: LGK 974 2.5 mg QD dosing	Escalation part: LGK 974 2.5 mg QD dosing	Escalation part: LGK 974 5 mg QD dosing	Escalation part: LGK 974 10 mg QD dosing	Expansion part: LGK 974 10 mg QD dosing	Expansion part: LGK 974 10 mg QD dosing

								dosing followed by 3-day break	of dosing followed by 3-day break			on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	on Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma that was primary refractory to prior anti-PD-1 therapy	on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma with acquired resistance to prior anti-PD-1 therapy
Number of Participa	6	6	10	11	10	6	5	4	3	5	28	5	4	4	11	5	14	8	25	15

nts Analyzed [units: participants]																				
Overall Response Rate (ORR) per RECIST v1.1 (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	0 (0.0 to 45.9)	0 (0.0 to 45.9)	0 (0.0 to 30.8)	0 (0.0 to 28.5)	0 (0.0 to 30.8)	0 (0.0 to 45.9)	0 (0.0 to 52.2)	0 (0.0 to 60.2)	0 (0.0 to 70.8)	0 (0.0 to 52.2)	0 (0.0 to 12.3)	0 (0.0 to 52.2)	0 (0.0 to 60.2)	0 (0.0 to 60.2)	9.1 (0.2 to 41.3)	20.0 (0.5 to 71.6)	7.1 (0.2 to 33.9)	12.5 (0.3 to 52.7)	20.0 (6.8 to 40.7)	0 (0.0 to 21.8)

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 according to RECIST v1.1. DOR is defined as the time from first observation of response to the first time of progression or death. If a participant had not had an event or when they received any further anticancer therapy, duration of overall response was censored at the date of last adequate tumor assessment. DOR was estimated using the Kaplan-Meier method.

NOVARTIS

Time Frame	Up to 0.5 years for LGK974 and 3.5 years for LGK974+PDR001
Analysis Population Description	All patients for whom best overall response is complete response (CR) or partial response (PR) per RECIST v1.1

	LGK 974 5mg QD	LGK 974 7.5 mg QD	LGK 974 10mg QD	LGK 974 15mg QD	LGK 974 20mg QD	LGK 974 22.5 mg QD	LGK 974 30mg QD	LGK 974 30mg 4/7 QD	LGK 974 45mg 4/7 QD	LGK 974 5mg BID	LGK 974 10mg QD Exp	LGK 974 2.5 mg QD C1 D1-8 + PDR 001	LGK 974 5mg QD C1 D1-8 + PDR 001	LGK 974 10mg QD C1 D1-8 + PDR 001	LGK 974 2.5 mg QD C1 D1-15 + PDR 001	LGK 974 2.5 mg QD C1-4 D1-8 + PDR 001	LGK 974 5mg QD C1-4 D1-8 + PDR 001	LGK 974 10mg QD C1-4 D1-8 + PDR 001	LGK 974 10mg QD C1-4 D1-8 + PDR 001 PrR	LGK 974 10mg QD C1-4 D1-8 + PDR 001 AR
Arm/ Group Description	Escalation part: LGK 974 5 mg QD	Escalation part: LGK 974 5 mg QD	Escalation part: LGK 974 10 mg QD	Escalation part: LGK 974 15 mg QD	Escalation part: LGK 974 20 mg QD	Escalation part: LGK 974 22.5 mg QD	Escalation part: LGK 974 30 mg QD	Escalation part: LGK 974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK 974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK 974 5 mg BID	Expansion part: LGK 974 10 mg QD	Escalation part: LGK 974 2.5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR 001	Escalation part: LGK 974 5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR 001	Escalation part: LGK 974 10 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR 001	Escalation part: LGK 974 2.5 mg QD dosing on Days 1 through 15 of Cycle 1 only and PDR	Escalation part: LGK 974 2.5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR	Escalation part: LGK 974 5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR	Escalation part: LGK 974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR	Expansion part: LGK 974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR	Expansion part: LGK 974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR

												400 mg Q4 W	400 mg Q4 W	400 mg Q4 W	001 400 mg Q4 W	001 400 mg Q4 W	001 400 mg Q4 W	001 400 mg Q4 W	001 400 mg Q4 W in cutaneous melanoma that was primary refractory to prior anti-PD-1 therapy	001 400 mg Q4 W in cutaneous melanoma with acquired resistance to prior anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	5	0
Duration of Resp	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**	**Median (95**

onse (DOR) per RECIST v1.1 (units: months)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)	% Confidence Interval)
																3.7 (NA to NA)[1]	19.3 (NA to NA)[1]	6.0 (NA to NA)[1]	NA (NA to NA)[1]	15.4 (3.5 to NA)[1]

[1] Not estimable due to insufficient number of participants with events.

Overall Response Rate (ORR) per irRC (Combination arm only)

Description	Tumor response was based on local investigator assessment as per immune-related response criteria (irRC). ORR per irRC is defined as the percentage of participants with a best overall response of Complete Response (irCR) or Partial Response (irPR). For irRC, irCR=Disappearance of all non-nodal target lesions and non-target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; irPR= At least a 30% decrease in the sum of diameters of all target lesions including new measurable lesions, taking as reference the baseline sum of diameters.
Time Frame	Up to 0.5 years for LGK974 and 3.5 years for LGK974+PDR001
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation or in the dose expansion.

LGK974 2.5mg QD C1 D1-8 + PDR001	LGK974 5mg QD C1 D1-8 + PDR001	LGK974 10mg QD C1 D1-8 + PDR001	LGK974 2.5mg QD C1 D1-15 + PDR001	LGK974 2.5mg QD C1-4 D1-8 + PDR001	LGK974 5mg QD C1-4 D1-8 + PDR001	LGK974 10mg QD C1-4 D1-8 + PDR001	LGK974 10mg QD C1-4 D1-8 + PDR001 PrR	LGK974 10mg QD C1-4 D1-8 + PDR001 AR

Arm/Group Description	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma that was primary refractory to prior anti-PD-1 therapy	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma with acquired resistance to prior anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	5	4	4	11	5	14	8	25	15
Overall Response Rate (ORR) per irRC (Combination arm only) (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	0 (0.0 to 52.2)	0 (0.0 to 60.2)	0 (0.0 to 60.2)	9.1 (0.2 to 41.3)	20.0 (0.5 to 71.6)	7.1 (0.2 to 33.9)	12.5 (0.3 to 52.7)	20.0 (6.8 to 40.7)	0 (0.0 to 21.8)

Duration of Response (DOR) per irRC (Combination arm only)

Description DOR only applies to patients for whom best overall response is complete response (irCR) or partial response (irPR) based on local investigator assessment according to irRC. DOR is defined as the time from first observation of response to the first time of progression or death. If a participant had not had an event or when they received any further anticancer therapy, duration of overall response was censored at the date of last adequate tumor assessment. DOR was estimated using the Kaplan-Meier method.

Time Frame	Up to 0.5 years for LGK974 and 3.5 years for LGK974+PDR001
Analysis Population Description	All patients for whom best overall response is complete response (irCR) or partial response (irPR) per irRC.

	LGK974 2.5mg QD C1 D1-8 + PDR001	LGK974 5mg QD C1 D1-8 + PDR001	LGK974 10mg QD C1 D1-8 + PDR001	LGK974 2.5mg QD C1 D1-15 + PDR001	LGK974 2.5mg QD C1-4 D1-8 + PDR001	LGK974 5mg QD C1-4 D1-8 + PDR001	LGK974 10mg QD C1-4 D1-8 + PDR001	LGK974 10mg QD C1-4 D1-8 + PDR001 PrR	LGK974 10mg QD C1-4 D1-8 + PDR001 AR
Arm/Group Description	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma that was primary refractory to prior anti-PD-1 therapy	Expansion part: LGK974 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W in cutaneous melanoma with acquired resistance to prior anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	0	0	0	1	1	1	1	5	0
Duration of Response (DOR) per irRC (Combination	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**

arm only) (units: months)					
	3.7 (NA to NA)[1]	25.8 (NA to NA)[1]	NA (NA to NA)[1]	NA (NA to NA)[1]	15.4 (3.5 to NA)[1]

[1] Not estimable due to insufficient number of participants with events.

Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of LGK974 – Single agent arm

Description	Pharmacokinetic (PK) parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUCinf calculation.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	4	6	35	9	9	6	5	4	2	1
Area under the plasma concentratio	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometric Mean**	**Geometri c Mean**

n-time curve from time zero to infinity (AUCinf) of LGK974 – Single agent arm (units: hr*ng/mL)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)	(Geometric Coefficient of Variation)
C1D1	259 (18.3 %)	301 (48.8 %)	470 (38.9 %)	635 (24.2 %)	1300 (34.9 %)	1040 (40.1 %)	1030 (65.7 %)	1770 (61.0 %)	3570 (17.6 %)	269

Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of LGK974 – Combination arm

Description	Pharmacokinetic (PK) parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUCinf calculation.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	LGK974 5mg QD + PDR001	LGK974 10mg QD + PDR001
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	8	10	8
Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of LGK974 – Combination arm (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**

C1D1	61.8 (41.5%)	153 (41.7%)	397 (47.5%)

Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LGK974 – Single agent arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUCtau calculation. The duration of the dosing interval (tau) was 24 hours for QD dosing and 12 hours for BID dosing.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 15 (C1D15)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	6	6	38	10	10	6	5	4	2	5
Area under the plasma concentration-time curve from time zero to the	**Geometric Mean (Geometric Coefficien**	**Geometric Mean (Geometric Coefficien**	**Geometric Mean (Geometric Coefficien**	**Geometric Mean (Geometric Coefficien**	**Geometric Mean (Geometric Coefficient**	**Geometric Mean (Geometric Coefficient**	**Geometric Mean (Geometric Coefficient**	**Geometric Mean (Geometric Coefficient**	**Geometric Mean (Geometric Coefficient**	**Geometric Mean (Geometric Coefficien**

end of the dosing interval (AUCtau) of LGK974 – Single agent arm (units: hr*ng/mL)	**t of Variation)**	**t of Variation)**	**t of Variation)**	**t of Variation)**	**of Variation)**	**of Variation)**	**of Variation)**	**of Variation)**	**of Variation)**	**t of Variation)**
C1D1	245 (9.8%)	290 (43.4 %)	434 (40.1 %)	567 (27.2 %)	1080 (27.2 %)	965 (33.8%)	928 (63.5%)	1680 (60.5 %)	3430 (13.9 %)	103 (64.1 %)
C1D15	294 (29.6 %)	443 (8.9%)	627 (37.7 %)	793 (36.0 %)	1630 (35.8 %)	1130 (45.2 %)	1880 (40.1 %)	2080 (71.7 %)	3690 (32.1 %)	141 (88.3 %)

Statistical Analysis

Groups	LGK974 5mg QD, LGK974 7.5mg QD, LGK974 10mg QD Esc+Exp, LGK974 15mg QD, LGK974 20mg QD, LGK974 22.5mg QD, LGK974 30mg QD	
Type of Statistical Test	Other	
Method	Other Power model	AUCtau values were analyzed using a power model: AUCtau=exp(alpha)*dose^beta
Slope	1.02	Dose proportionality was concluded across the whole dose range (5-30 mg) if the 90% CI for the slope (beta) was contained within a pre-specified range (0.875, 1.125).
90 % Confidence Interval 2-Sided	0.85 to 1.20	

Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LGK974 – Combination arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUCtau calculation. The duration of the dosing interval (tau) was 24 hours for QD dosing.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 8 (C1D8)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	20	15	11
Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LGK974 – Combination arm (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	81.5 (35.0%)	155 (49.8%)	368 (38.5%)
C1D8	112 (42.8%)	234 (27.2%)	489 (45.0%)

Maximum observed plasma concentration (Cmax) of LGK974 – Single agent arm

Description	PK parameters were calculated based on LGK974 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, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 15 (C1D15)). One cycle=28 days.

Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	6	6	38	10	10	6	5	4	3	5
Maximum observed plasma concentration (Cmax) of LGK974 – Single agent arm (units: ng/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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	33.0 (26.4 %)	48.1 (47.7 %)	72.6 (51.0 %)	90.9 (29.0 %)	144 (24.6%)	178 (40.2%)	143 (64.5%)	209 (46.1%)	473 (88.6%)	25.6 (65.2 %)
C1D15	33.4 (52.9 %)	61.4 (55.1 %)	85.6 (55.1 %)	128 (46.5%)	197 (38.2%)	191 (56.0%)	251 (64.6%)	260 (52.5%)	373 (51.4%)	31.3 (94.5 %)

Statistical Analysis

Groups	LGK974 5mg QD, LGK974 7.5mg QD, LGK974 10mg QD Esc+Exp, LGK974 15mg QD, LGK974 20mg QD, LGK974 22.5mg QD, LGK974 30mg QD	
Type of Statistical Test	Other	
Method	Other Power model	Cmax values were analyzed using a power model: Cmax=exp(alpha)*dose^beta
Slope	1.11	Dose proportionality was concluded across the whole dose range (5-30 mg) if the 90% CI for the slope (beta) was contained within a pre-specified range (0.875, 1.125).
90 % Confidence Interval 2-Sided	0.88 to 1.34	

Maximum observed plasma concentration (Cmax) of LGK974 – Combination arm

Description	PK parameters were calculated based on LGK974 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, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 8 (C1D8)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W

Number of Participants Analyzed [units: participants]	20	15	11
Maximum observed plasma concentration (Cmax) of LGK974 – Combination arm (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	14.0 (37.4%)	31.5 (57.5%)	57.1 (45.7%)
C1D8	18.6 (33.0%)	36.5 (50.2%)	79.7 (45.8%)

Time to reach maximum plasma concentration (Tmax) of LGK974 – Single agent arm

Description	PK parameters were calculated based on LGK974 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, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 15 (C1D15)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	6	6	38	10	10	6	5	4	3	5

Time to reach maximum plasma concentration (Tmax) of LGK974 – Single agent arm (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
C1D1	1.98 (1.00 to 4.00)	2.00 (2.00 to 4.00)	1.75 (0.467 to 4.00)	2.00 (1.00 to 3.05)	2.02 (0.967 to 4.05)	1.00 (0.500 to 3.00)	1.00 (0.500 to 3.13)	2.50 (2.00 to 3.03)	1.00 (0.500 to 6.00)	3.00 (2.00 to 3.17)
C1D15	2.98 (0.500 to 3.00)	1.00 (0.500 to 4.08)	2.00 (0.500 to 4.00)	2.50 (0.500 to 3.00)	2.00 (0.500 to 3.00)	1.00 (1.00 to 1.05)	1.00 (1.00 to 1.00)	2.50 (2.00 to 6.10)	4.00 (1.00 to 6.00)	3.00 (1.00 to 4.00)

Time to reach maximum plasma concentration (Tmax) of LGK974 – Combination arm

Description	PK parameters were calculated based on LGK974 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, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 8 (C1D8)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	20	15	11

Time to reach maximum plasma concentration (Tmax) of LGK974 – Combination arm (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
C1D1	1.79 (0.933 to 4.90)	1.00 (0.500 to 2.95)	2.18 (0.833 to 6.00)
C1D8	1.04 (0.500 to 5.33)	1.00 (0.500 to 3.08)	2.00 (0.483 to 2.95)

Minimum observed plasma concentration (Cmin) of LGK974 – Single agent arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. Cmin is defined as the minimum concentration of a drug during a dosing interval.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after dosing at steady state (Cycle 1 Day 15 (C1D15)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	4	5	31	8	7	4	4	4	3	4

Minimum observed plasma concentration (Cmin) of LGK974 – Single agent arm (units: ng/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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D15	2.40 (56.6 %)	3.91 (66.3 %)	4.56 (60.2 %)	4.92 (42.5 %)	16.4 (161.9 %)	10.5 (106.9 %)	17.1 (68.0 %)	2.67 (81.8 %)	2.99 (81.0 %)	4.71 (134.5 %)

Minimum observed plasma concentration (Cmin) of LGK974 – Combination arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. Cmin is defined as the minimum concentration of a drug during a dosing interval.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after dosing at steady state (Cycle 1 Day 8 (C1D8)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	20	15	9
Minimum observed plasma concentration (Cmin) of LGK974 – Combination arm (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D8	1.57 (87.3%)	1.38 (19.8%)	3.02 (58.4%)

Terminal elimination half-life (T1/2) of LGK974 – Single agent arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. Elimination half-life (T1/2) values were calculated as 0.693/terminal elimination rate constant.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 15 (C1D15)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	6	6	37	10	10	6	5	4	2	4
Terminal elimination half-life (T1/2) of LGK974 – Single agent arm	**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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**

(units: hours)										
C1D1	4.25 (47.4 %)	5.14 (42.8 %)	6.03 (45.7 %)	5.75 (34.1 %)	7.06 (54.5 %)	6.50 (33.5 %)	7.57 (59.8 %)	5.42 (26.6 %)	5.34 (32.2 %)	12.6 (20.9 %)
C1D15	6.75 (31.6 %)	6.82 (15.1 %)	6.22 (22.4 %)	6.18 (14.4 %)	7.39 (44.5 %)	7.49 (53.4 %)	7.79 (53.4 %)	6.31 (12.7 %)	5.35 (15.8 %)	4.84 (20.5 %)

Terminal elimination half-life (T1/2) of LGK974 – Combination arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. Elimination half-life (T1/2) values were calculated as 0.693/terminal elimination rate constant.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 8 (C1D8)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	16	15	8
Terminal elimination half-life (T1/2) of LGK974 – Combination arm (units: hours)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	3.32 (38.8%)	3.08 (37.1%)	5.56 (47.2%)
C1D8	5.11 (50.4%)	6.59 (53.5%)	5.09 (37.2%)

Accumulation ratio (Racc) of LGK974 – Single agent arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. Racc was calculated as the ratio between AUCtau on C1D15 and AUCtau on C1D1.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	4	5	30	8	6	4	4	3	2	4
Accumulation ratio (Racc) of LGK974 – Single agent arm (units: ratio)	**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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D15	1.16 (21.0 %)	1.31 (26.2 %)	1.50 (34.5 %)	1.50 (35.7 %)	1.58 (52.6 %)	1.18 (32.9 %)	1.67 (16.8 %)	1.18 (11.1 %)	1.08 (17.6 %)	1.60 (27.6 %)

Accumulation ratio (Racc) of LGK974 – Combination arm

Description	PK parameters were calculated based on LGK974 plasma concentrations by using non-compartmental methods. Racc was calculated as the ratio between AUCtau on C1D8 and AUCtau on C1D1.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose (Cycle 1 Day 1 (C1D1)) and after dosing at steady state (Cycle 1 Day 8 (C1D8)). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	19	14	9
Accumulation ratio (Racc) of LGK974 – Combination arm (units: ratio)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D8	1.40 (34.6%)	1.45 (44.6%)	1.22 (29.1%)

Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of LHA333 – Single agent arm

Description	PK parameters were calculated based on the plasma concentrations of LHA333, an active metabolite of LGK974, by using non-compartmental methods. The linear trapezoidal method was used for AUCinf calculation.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	0	5	25	8	7	6	5	4	2	0
Area under the plasma concentration -time curve from time zero to infinity (AUCinf) of LHA333 – Single agent arm (units: hr*ng/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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1		165 (33.1%)	264 (42.7%)	381 (49.8%)	543 (27.0%)	512 (31.2%)	528 (69.2%)	867 (34.3%)	2030 (3.3%)	

Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of LHA333 – Combination arm

Description	PK parameters were calculated based on the plasma concentrations of LHA333, an active metabolite of LGK974, by using non-compartmental methods. The linear trapezoidal method was used for AUCinf calculation.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	LGK974 5mg QD + PDR001	LGK974 10mg QD + PDR001
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	0	3	7
Area under the plasma concentration-time curve from time zero to infinity (AUCinf) of LHA333 – Combination arm (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1		103 (38.9%)	262 (37.8%)

Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LHA333 – Single agent arm

Description	PK parameters were calculated based on the plasma concentrations of LHA333, an active metabolite of LGK974, by using non-compartmental methods. The linear trapezoidal method was used for AUCtau calculation. The duration of the dosing interval (tau) was 24 hours for QD dosing and 12 hours for BID dosing.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1) and after dosing at steady state (C1D15). One cycle=28 days.

Analysis Population Description: Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	6	6	34	9	10	6	5	4	2	5
Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LHA333 – Single agent arm (units: hr*ng/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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	54.2 (55.4 %)	149 (33.2 %)	208 (50.9 %)	333 (46.3 %)	426 (37.3 %)	457 (28.5 %)	458 (68.9 %)	802 (33.4 %)	1910 (1.2%)	36.7 (81.3%)

C1D15	95.7 (84.4 %)	119 (18.4 %)	223 (53.7 %)	345 (42.2 %)	657 (35.4 %)	367 (49.3 %)	644 (80.0 %)	810 (44.0 %)	1530 (59.2 %)	34.1 (124.2 %)

Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LHA333 – Combination arm

Description	PK parameters were calculated based on the plasma concentrations of LHA333, an active metabolite of LGK974, by using non-compartmental methods. The linear trapezoidal method was used for AUCtau calculation. The duration of the dosing interval (tau) was 24 hours for QD dosing.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1) and after dosing at steady state (C1D8). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	20	14	11
Area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUCtau) of LHA333 – Combination arm (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	33.1 (44.8%)	62.8 (40.2%)	175 (61.1%)
C1D8	32.4 (79.2%)	78.1 (46.7%)	176 (79.6%)

Maximum observed plasma concentration (Cmax) of LHA333 – Single agent arm

Description	PK parameters were calculated based on the plasma concentrations of LHA333, an active metabolite of LGK974, 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, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1) and after dosing at steady state (C1D15). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	6	6	38	10	10	6	5	4	3	5
Maximum observed plasma concentration (Cmax) of LHA333 – Single agent arm (units: ng/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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	5.61 (35.1 %)	12.0 (43.8 %)	19.1 (64.1 %)	26.9 (63.6 %)	37.5 (76.7 %)	48.9 (47.4 %)	41.2 (84.3%)	72.6 (36.5 %)	129 (179.8 %)	6.88 (71.2 %)
C1D15	6.17 (66.1 %)	9.39 (68.1 %)	18.0 (74.6 %)	29.7 (42.3 %)	51.6 (57.4 %)	34.6 (75.7 %)	46.4 (104.0 %)	62.9 (47.4 %)	87.2 (80.6%)	5.65 (86.2 %)

Maximum observed plasma concentration (Cmax) of LHA333 – Combination arm

Description	PK parameters were calculated based on the plasma concentrations of LHA333, an active metabolite of LGK974, 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, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1) and after dosing at steady state (C1D8). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	20	15	11
Maximum observed plasma concentration (Cmax) of LHA333 – Combination arm (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1	3.55 (39.9%)	7.45 (56.4%)	15.7 (55.8%)
C1D8	3.72 (49.3%)	7.06 (42.5%)	18.5 (63.4%)

Metabolite-to-parent (M/P) ratio – Single agent arm

Description	PK parameters were calculated based on the plasma concentrations of LGK974 and its active metabolite LHA333 by using non-compartmental methods. The M/P ratio was calculated by dividing the AUC of the metabolite by the AUC of the parent drug, considering AUCinf on C1D1 and AUCtau on C1D15.
Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1) and after dosing at steady state (C1D15). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure in each timepoint. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	2	5	27	8	7	6	5	4	2	4
Metabolite-to-parent (M/P) ratio – Single agent arm (units: ratio)	**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)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1		0.518 (88.9 %)	0.498 (34.0 %)	0.578 (55.8 %)	0.415 (57.2 %)	0.472 (25.9 %)	0.494 (29.7 %)	0.470 (41.6 %)	0.547 (14.2 %)	
C1D15	0.250 (86.7 %)	0.264 (10.5 %)	0.335 (49.2 %)	0.418 (53.3 %)	0.385 (55.0 %)	0.314 (52.6 %)	0.309 (34.5 %)	0.374 (26.7 %)	0.397 (23.8 %)	0.233 (32.5 %)

Metabolite-to-parent (M/P) ratio – Combination arm

Description PK parameters were calculated based on the plasma concentrations of LGK974 and its active metabolite LHA333 by using non-compartmental methods. The M/P ratio was calculated by dividing the AUC of the metabolite by the AUC of the parent drug, considering AUCinf on C1D1 and AUCtau on C1D8.

Time Frame	pre-dose, 0.5, 1, 2, 3, 4, 6, 8 and 24 hours after first dose of LGK974 (C1D1) and after dosing at steady state (C1D8). One cycle=28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	**LGK974 5mg QD + PDR001**	**LGK974 10mg QD + PDR001**
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	20	14	8
Metabolite-to-parent (M/P) ratio – Combination arm (units: ratio)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
C1D1		0.721 (92.1%)	0.647 (68.7%)
C1D8	0.277 (57.2%)	0.325 (45.6%)	0.380 (43.9%)

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 spartalizumab serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUClast calculation.
Time Frame	pre-infusion and 1, 24, 168, 336 and 672 hours after completion of the PDR001 infusion on C1D1. The duration of the infusion was 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	LGK974 5mg QD + PDR001	LGK974 10mg QD + PDR001
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	18	18	48
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)**
Cycle 1	24900 (22.5%)	22100 (45.8%)	24300 (58.6%)

Maximum observed serum concentration (Cmax) of PDR001

Description	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 and 1, 24, 168, 336 and 672 hours after completion of the PDR001 infusion on C1D1. The duration of the infusion was 30 minutes. The duration of one cycle was 28 days.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) with an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	LGK974 2.5mg QD + PDR001	LGK974 5mg QD + PDR001	LGK974 10mg QD + PDR001
Arm/Group Description	Escalation part: LGK974 2.5 mg QD (C1 D1-8, C1 D1-15 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation part: LGK974 5 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W	Escalation and expansion: LGK974 10 mg QD (C1 D1-8 and C1-4 D1-8) and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	18	18	48

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)
Cycle 1	89.7 (24.8%)	85.9 (31.3%)	92.5 (32.9%)

Percentage change from baseline in AXIN2 mRNA expression in tumor biopsies (Single agent arm only)

Description	Change from baseline in AXIN2 gene expression levels were assessed by measuring AXIN2 mRNA in paired tumor biopsies.
Time Frame	Baseline (before first dose of LGK974) and during treatment (once in the first cycle between Day 5 and Day 28 following 5 consecutive days of LGK974 treatment).
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation part and had a valid assessment for the outcome measure.

	LGK974 5mg QD	LGK974 7.5mg QD	LGK974 10mg QD Esc+Exp	LGK974 15mg QD	LGK974 20mg QD	LGK974 22.5mg QD	LGK974 30mg QD	LGK974 30mg 4/7 QD	LGK974 45mg 4/7 QD	LGK974 5mg BID
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK974 5 mg BID
Number of Participants Analyzed [units: participants]	1	3	13	1	2	1	3	1	1	3
Percentage change from baseline in AXIN2 mRNA	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**

expression in tumor biopsies (Single agent arm only) (units: % change from baseline in mRNA)										
	-17.01 (-17.01 to -17.01)	-21.92 (-90.4 to 179.3)	-32.92 (-81.1 to 185.4)	-24.06 (-24.06 to -24.06)	57.28 (-24.1 to 138.7)	1.89 (1.89 to 1.89)	-66.94 (-87.6 to -40.1)	-80.15 (-80.15 to -80.15)	-80.90 (-80.90 to -80.90)	-71.66 (-83.1 to -11.2)

Percentage change from baseline in AXIN2 mRNA expression in skin biopsies

Description	Change from baseline in AXIN2 gene expression levels were assessed by measuring AXIN2 mRNA in paired skin biopsies.
Time Frame	Baseline (before first dose of LGK974) and during treatment (once in the first cycle between Day 5 and Day 28 following 5 consecutive days of LGK974 treatment).
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation part and had a valid assessment for the outcome measure.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+ Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**	**LGK974 2.5mg QD C1 D1-8 + PDR001**	**LGK974 5mg QD C1 D1-8 + PDR001**	**LGK974 10mg QD C1 D1-8 + PDR001**	**LGK974 2.5mg QD C1 D1-15 + PDR001**	**LGK974 2.5mg QD C1-4 D1-8 + PDR001**	**LGK974 5mg QD C1-4 D1-8 + PDR001**	**LGK974 10mg QD C1-4 D1-8 + PDR001 Esc+ Exp**
Arm/Group Description	Escalation part: LGK974 5	Escalation part: LGK974 5	Escalation and expansion: LGK9	Escalation part: LGK974 15	Escalation part: LGK974 20	Escalation part: LGK974 22.5	Escalation part: LGK974 30	Escalation part: LGK974 30 mg, 4	Escalation part: LGK974 45 mg	Escalation part: LGK974 5	Escalation part: LGK974 2.5	Escalation part: LGK974 5 mg	Escalation part: LGK974 10 mg	Escalation part: LGK974 2.5	Escalation part: LGK974 2.5	Escalation part: LGK974 5 mg	Escalation and expansion: LGK9

	mg QD	mg QD	74 10 mg QD	mg QD	mg QD	mg QD	mg QD	days of dosing followed by 3-day break	QD, 4 days of dosing followed by 3-day break	mg BID	mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	QD dosing on Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	mg QD dosing on Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	74 10 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	4	4	14	6	8	4	4	2	3	4	4	2	2	9	4	9	3
Percentage change from baseline in AXIN2 mRNA expression in skin biopsies (units:	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**

% change from baseline in mRNA)																
	-35.79 (-67.7 to 91.2)	-71.93 (-88.3 to 4.8)	-53.12 (-82.9 to -17.8)	-50.98 (-88.3 to 97.6)	-62.66 (-86.2 to 2.4)	-58.72 (-62.3 to -27.8)	-6.08 (-78.2 to 67.1)	-60.09 (-90.9 to -29.3)	-52.58 (-78.9 to 5.7)	-54.08 (-78.7 to -6.6)	-46.82 (-55.9 to -28.7)	-65.19 (-65.8 to -64.6)	-46.75 (-53.5 to -40.0)	-51.80 (-72.9 to 98.2)	-19.52 (-42.4 to 11.3)	-52.50 (-77.4 to -12.9)	-55.86 (-76.2 to -35.7)

Exposure-response (ER) relationship: Maximal effect (Emax) of LGK974 to inhibit skin AXIN2 calculated by Emax model

Description	The ER relationship of LGK974 Cmin versus skin AXIN2 mRNA expression was appropriately described by a maximum effect (Emax) model. The estimated median of the parameter and 90% prediction interval are summarized in the table.
Time Frame	Baseline (before first dose of LGK974) and during treatment (once in the first cycle between Day 5 and Day 28 following 5 consecutive days of LGK974 treatment).
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation part and had a valid assessment for the model

	Model-estimated parameters
Arm/Group Description	Model-estimated parameters for exposure-response analysis of LGK974 Cmin and skin AXIN2 reduction at steady state following QD dosing of LGK974 at single agent in dose escalation
Number of Participants Analyzed [units: participants]	49
Exposure-response (ER) relationship: Maximal effect (Emax) of LGK974 to inhibit skin AXIN2 calculated by Emax model (units: % of skin AXIN2 inhibition)	**Median (90% Confidence Interval)**

62.9
(46.7 to 78.4)

Exposure-response (ER) relationship: Concentration of LGK974 that produces 50% of the maximum effect (EC50) calculated by Emax model

Description	The ER relationship of LGK974 Cmin versus skin AXIN2 mRNA expression was appropriately described by a maximum effect (Emax) model. The estimated median of the parameter and 90% prediction interval are summarized in the table.
Time Frame	Baseline (before first dose of LGK974) and during treatment (once in the first cycle between Day 5 and Day 28 following 5 consecutive days of LGK974 treatment).
Analysis Population Description	All patients who received at least one dose of study treatment in the dose escalation part and had a valid assessment for the model

	Model-estimated parameters
Arm/Group Description	Model-estimated parameters for exposure-response analysis of LGK974 Cmin and skin AXIN2 reduction at steady state following QD dosing of LGK974 at single agent in dose escalation
Number of Participants Analyzed [units: participants]	49
Exposure-response (ER) relationship: Concentration of LGK974 that produces 50% of the maximum effect (EC50) calculated by Emax model (units: ng/mL)	**Median (90% Confidence Interval)**
	0.484 (0.123 to 1.96)

NOVARTIS

Post-Hoc Outcome Result(s)

All-Collected Deaths

Description	On-treatment deaths were collected from the first dose of the study drug up to 30 days after the last dose. Post-treatment deaths were collected from 31 days after the last dose until a maximum of 150 days after the last dose. All deaths refer to the sum of on-treatment and post-treatment deaths.
Time Frame	On-treatment deaths: up to approximately 0.6 years for LGK974 single agent and 3.6 years for LGK974 in combination with PDR001. Post-treatment deaths: up to approximately 0.7 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001.
Analysis Population Description	All patients who received at least one dose of study drug.

	LGK974 5mg QD	**LGK974 7.5mg QD**	**LGK974 10mg QD Esc+ Exp**	**LGK974 15mg QD**	**LGK974 20mg QD**	**LGK974 22.5 mg QD**	**LGK974 30mg QD**	**LGK974 30mg 4/7 QD**	**LGK974 45mg 4/7 QD**	**LGK974 5mg BID**	**LGK974 2.5mg QD C1 D1-8 + PDR001**	**LGK974 5mg QD C1 D1-8 + PDR001**	**LGK974 10mg QD C1 D1-8 + PDR001**	**LGK974 2.5mg QD C1 D1-15 + PDR001**	**LGK974 2.5mg QD C1-4 D1-8 + PDR001**	**LGK974 5mg QD C1-4 D1-8 + PDR001**	**LGK974 10mg QD C1-4 D1-8 + PDR001 Esc+ Exp**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by	Escalation part: LGK974 5 mg BID	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of	Escalation part: LGK974 10 mg QD dosing on Days 1 through 8 of	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 15	Escalation part: LGK974 2.5 mg QD dosing on Days 1 through 8	Escalation part: LGK974 5 mg QD dosing on Days 1 through 8 of	Escalation and expansion: LGK974 10 mg QD dosing on Days 1 throug

									3-day break		of Cycle 1 only and PDR001 400 mg Q4W	Cycle 1 only and PDR001 400 mg Q4W	Cycle 1 only and PDR001 400 mg Q4W	of Cycle 1 only and PDR001 400 mg Q4W	of each Cycle 1 to 4 and PDR001 400 mg Q4W	each Cycle 1 to 4 and PDR001 400 mg Q4W	h 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W
Number of Participants Analyzed [units: participants]	6	6	38	11	10	6	5	4	3	5	5	4	4	11	5	14	48
All-Collected Deaths (units: participants)																	
On-treatment deaths	2	0	6	3	2	1	2	1	1	0	0	0	0	1	0	1	4
Post-treatment deaths	0	0	3	0	0	0	0	0	0	0	1	0	1	2	1	5	9
All deaths	2	0	9	3	2	1	2	1	1	0	1	0	1	3	1	6	13

Safety Results

Time Frame	Adverse events: from the first dose of study drug to 30 days after last dose (LGK974 single agent) and to 150 days after last dose (LGK974+PDR001), up to approximately 0.6 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001. All deaths: from the first dose of study treatment until a maximum of 150 days after the last dose, up to approximately 0.7 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001.
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	LGK 974 5mg QD N = 6	**LGK 974 7.5mg QD N = 6**	**LGK974 10mg QD Esc+ Exp N = 38**	**LGK 974 15mg QD N = 11**	**LGK 974 20mg QD N = 10**	**LGK 974 22.5 mg QD N = 6**	**LGK 974 30mg QD N = 5**	**LGK 974 30mg 4/7 QD N = 4**	**LGK 974 45mg 4/7 QD N = 3**	**LGK 974 5mg BID N = 5**	**LGK 974 2.5mg QD C1 D1-8 + PDR 001 N = 5**	**LGK 974 5mg QD C1 D1-8 + PDR 001 N = 4**	**LGK 974 10mg QD C1 D1-8 + PDR 001 N = 4**	**LGK 974 2.5mg QD C1 D1-15 + PDR 001 N = 11**	**LGK 974 2.5mg QD C1-4 D1-8 + PDR 001 N = 5**	**LGK 974 5mg QD C1-4 D1-8 + PDR 001 N = 14**	**LGK974 10mg QD C1-4 D1-8 + PDR001 Esc+ Exp N = 48**	**All patients N = 185**
Arm/Group Description	Escalation part: LGK974 5 mg QD	Escalation part: LGK974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK974 15 mg QD	Escalation part: LGK974 20 mg QD	Escalation part: LGK974 22.5 mg QD	Escalation part: LGK974 30 mg QD	Escalation part: LGK974 30 mg, 4 days of dosing	Escalation part: LGK974 45 mg QD, 4 days of	Escalation part: LGK974 5 mg BID	Escalation part: LGK974 2.5 mg QD dosing on	Escalation part: LGK974 5 mg QD dosing on Days	Escalation part: LGK974 10 mg QD dosing on Days	Escalation part: LGK974 2.5 mg QD dosing on	Escalation part: LGK974 2.5 mg QD dosing on	Escalation part: LGK974 5 mg QD dosing on Days	Escalation and expansion: LGK974 10 mg QD dosin	All patients

								followed by 3-day break	dosing followed by 3-day break		Days 1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	Days 1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	g on Days 1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	
Total Number Affected	2	0	9	3	2	1	2	1	1	0	1	0	1	3	1	6	13	46
Total Number At Risk	6	6	38	11	10	6	5	4	3	5	5	4	4	11	5	14	48	185

Serious Adverse Events

Time Frame	Adverse events: from the first dose of study drug to 30 days after last dose (LGK974 single agent) and to 150 days after last dose (LGK974+PDR001), up to approximately 0.6 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001. All deaths: from the first dose of study treatment until a maximum of 150 days after the last dose, up to approximately 0.7 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001.
Source Vocabulary for Table Default	MedDRA (27.0)

Collection Approach for Table Default Systematic Assessment

	LGK 974 5mg QD N = 6	LGK 974 7.5mg QD N = 6	LGK 974 10mg QD Esc+ Exp N = 38	LGK 974 15mg QD N = 11	LGK 974 20mg QD N = 10	LGK 974 22.5 mg QD N = 6	LGK 974 30mg QD N = 5	LGK 974 30mg 4/7 QD N = 4	LGK9 74 45mg 4/7 QD N = 3	LGK 974 5mg BID N = 5	LGK 974 2.5mg QD C1 D1-8 + PDR 001 N = 5	LGK 974 5mg QD C1 D1-8 + PDR 001 N = 4	LGK 974 10mg QD C1 D1-8 + PDR 001 N = 4	LGK 974 2.5 mg QD C1 D1-15 + PDR 001 N = 11	LGK 974 2.5mg QD C1-4 D1-8 + PDR 001 N = 5	LGK 974 5mg QD C1-4 D1-8 + PDR 001 N = 14	LGK 974 10mg QD C1-4 D1-8 + PDR 001 Esc+ Exp N = 48	All patients N = 185
Arm/Group Description	Escalation part: LGK 974 5 mg QD	Escalation part: LGK 974 5 mg QD	Escalation and expansion: LGK 974 10 mg QD	Escalation part: LGK 974 15 mg QD	Escalation part: LGK 974 20 mg QD	Escalation part: LGK 974 22.5 mg QD	Escalation part: LGK 974 30 mg QD	Escalation part: LGK 974 30 mg, 4 days of dosing followed by 3-day break	Escalation part: LGK9 74 45 mg QD, 4 days of dosing followed by 3-day break	Escalation part: LGK 974 5 mg BID	Escalation part: LGK 974 2.5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR	Escalation part: LGK 974 5 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR 001	Escalation part: LGK 974 10 mg QD dosing on Days 1 through 8 of Cycle 1 only and PDR	Escalation part: LGK 974 2.5 mg QD dosing on Days 1 through 15 of Cycle 1 only	Escalation part: LGK 974 2.5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4 and	Escalation part: LGK 974 5 mg QD dosing on Days 1 through 8 of each Cycle 1 to 4	Escalation and expansion: LGK 974 10 mg QD dosing on Days 1 through 8 of	All patients

											001 400 mg Q4W	400 mg Q4W	001 400 mg Q4W	and PDR 001 400 mg Q4 W	PDR 001 400 mg Q4W	and PDR 001 400 mg Q4 W	each Cycl e 1 to 4 and PDR 001 400 mg Q4W	
Total # Affected by any Serious Adverse Event	3	4	22	5	7	4	4	2	3	1	3	4	1	2	4	7	13	89
Total # at Risk by any Serious Adverse Event	6	6	38	11	10	6	5	4	3	5	5	4	4	11	5	14	48	185
Blood and lymphatic system disorders																		
Anaemia	0 (0. 00%)	0 (0. 00%)	1 (2. 63%)	0 (0. 00%)	0 (0. 00%)	1 (16 .67%)	0 (0. 00%)	0 (0. 00%)	0 (0.0 0%)	0 (0. 00%)	0 (0. 00%)	1 (25 .00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	3 (1. 62%)
Thromboc ytopenia	0 (0. 00%)	0 (0. 00%)	1 (2. 63%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0.0 0%)	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 (0. 54%)
Cardiac disorders																		
Atrial fibrillation	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0.0 0%)	0 (0. 00%)	0 (0. 00%)	1 (25 .00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	0 (0. 00%)	1 (0. 54%)

Cardiac arrest	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Endocrine disorders																		
Adrenal insufficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
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 (25.00%)	0 (0.00%)	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 (0.54%)
Abdominal pain	1 (16.67%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Ascites	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Colitis	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Constipation	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Diarrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Enteritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)

Enterovesical 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Faecaloma	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Gastric perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Immune-mediated gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Intestinal haemorrhage	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Intestinal obstruction	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Intestinal perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Mouth haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Nausea	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	5 (2.70%)
Small intestinal obstruction	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)

Subileus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Upper gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Vomiting	0 (0.00%)	0 (0.00%)	4 (10.53%)	1 (9.09%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	8 (4.32%)
General disorders and administration site conditions																		
Asthenia	0 (0.00%)	1 (16.67%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (2.70%)
Catheter site haemorrhage	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Chills	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Fatigue	0 (0.00%)	0 (0.00%)	1 (2.63%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
General physical health deterioration	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	2 (1.08%)

Malaise	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Pyrexia	0 (0.00%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	5 (2.70%)
Hepatobiliary disorders																	
Biliary dilatation	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Biliary obstruction	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Cholangitis	0 (0.00%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Hepatic failure	1 (16.67%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Hyperbilirubinaemia	0 (0.00%)	0 (0.00%)	1 (2.63%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
Jaundice	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)

Infections and infestations																	
Device related infection	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Hepatic infection	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Infected skin ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Pneumonia	0 (0.00%)	0 (0.00%)	1 (2.63%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Staphylococcal bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Urinary tract 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (1.08%)
Injury, poisoning and procedural complications																	
Brain herniation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	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 (0.54%)

Clavicle fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Craniocerebral 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
Spinal compression fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Spinal fracture	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Investigations																	
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	4 (2.16%)
Blood calcium increased	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Metabolism and nutrition disorders																	
Cachexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Decreased appetite	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	3 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (2.70%)

Diabetes mellitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Diabetic ketoacidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Failure to thrive	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Hypercalcaemia	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (2.70%)
Hyperglycaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Hypoglycaemia	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	1 (2.63%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Hypophosphataemia	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 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Malnutrition	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 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Musculoskeletal and connective tissue disorders																	

Arthralgia	0 (0.00%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Back pain	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Muscular weakness	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Myalgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Neck pain	0 (0.00%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Pathological fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	1 (0.54%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)																		
Cancer pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Metastases to central nervous system	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	2 (1.08%)

Tumour pain	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	3 (1.62%)
Nervous system disorders																		
Aphasia	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
Dysgeusia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Epilepsy	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Sacral radiculopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Seizure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Spinal cord compression	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Product issues																		
Device malfunction	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Psychiatric disorders																		

Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (33.33%)	1 (20.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	5 (2.70%)
Mental status changes	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 (33.33%)	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 (0.54%)
Renal and urinary disorders																		
Acute kidney injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (1.08%)
Renal failure	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)
Renal impairment	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)
Respiratory, thoracic and mediastinal disorders																		
Dyspnoea	1 (16.67%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	3 (6.25%)	11 (5.95%)
Pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	1 (2.08%)	3 (1.62%)
Productive cough	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)
Pulmonary embolism	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)

Pulmonary thrombosis	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)
Respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)
Skin and subcutaneous tissue disorders																		
Decubitus ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Vascular disorders																		
Deep vein thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	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 (0.54%)
Haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Hypotension	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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 (1.08%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events: from the first dose of study drug to 30 days after last dose (LGK974 single agent) and to 150 days after last dose (LGK974+PDR001), up to approximately 0.6 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001. All deaths: from the first dose of study treatment until a maximum of 150 days after the last dose, up to approximately 0.7 years for LGK974 single agent and 3.9 years for LGK974 in combination with PDR001.

Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	LGK 974 5mg QD N = 6	**LGK 974 7.5mg QD N = 6**	**LGK 974 10mg QD Esc+ Exp N = 38**	**LGK 974 15mg QD N = 11**	**LGK 974 20mg QD N = 10**	**LGK 974 22.5 mg QD N = 6**	**LGK 974 30mg QD N = 5**	**LGK 974 30mg 4/7 QD N = 4**	**LGK 974 45mg 4/7 QD N = 3**	**LGK 974 5mg BID N = 5**	**LGK 974 2.5mg QD C1 D1-8 + PDR 001 N = 5**	**LGK 974 5mg QD C1 D1-8 + PDR 001 N = 4**	**LGK 974 10mg QD C1 D1-8 + PDR 001 N = 4**	**LGK 974 2.5mg QD C1 D1-15 + PDR 001 N = 11**	**LGK 974 2.5mg QD C1-4 D1-8 + PDR 001 N = 5**	**LGK 974 5mg QD C1-4 D1-8 + PDR 001 N = 14**	**LGK 974 10mg QD C1-4 D1-8 + PDR 001 Esc+ Exp N = 48**	**All patients N = 185**
Arm/Group Description	Escalation part: LGK 974 5 mg QD	Escalation part: LGK 974 5 mg QD	Escalation and expansion: LGK974 10 mg QD	Escalation part: LGK 974 15 mg QD	Escalation part: LGK 974 20 mg QD	Escalation part: LGK 974 22.5 mg QD	Escalation part: LGK 974 30 mg QD	Escalation part: LGK 974 30 mg, 4 days of dosing	Escalation part: LGK974 45 mg QD, 4 days of dosing followed by	Escalation part: LGK 974 5 mg BID	Escalation part: LGK 974 2.5 mg QD dosing on Days	Escalation part: LGK 974 5 mg QD dosing on Days 1	Escalation part: LGK 974 10 mg QD dosing on Days	Escalation part: LGK 974 2.5 mg QD dosing on Days	Escalation part: LGK 974 2.5 mg QD dosing on Days	Escalation part: LGK 974 5 mg QD dosing on Days 1	Escalation and expansion: LGK974 10 mg QD dosing on Days	All patients

								followed by 3-day break	3-day break		1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	through 8 of Cycle 1 only and PDR001 400 mg Q4W	1 through 8 of Cycle 1 only and PDR001 400 mg Q4W	1 through 15 of Cycle 1 only and PDR001 400 mg Q4W	1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	1 through 8 of each Cycle 1 to 4 and PDR001 400 mg Q4W	
Total # Affected by any Other Adverse Event	6	6	38	11	10	6	5	4	3	5	5	4	4	11	5	14	47	184
Total # at Risk by any Other Adverse Event	6	6	38	11	10	6	5	4	3	5	5	4	4	11	5	14	48	185
Blood and lymphatic system disorders																		
Anaemia	0 (0.00%)	5 (83.33%)	13 (34.21%)	3 (27.27%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (60.00%)	1 (20.00%)	1 (25.00%)	1 (25.00%)	2 (18.18%)	0 (0.00%)	3 (21.43%)	8 (16.67%)	41 (22.16%)
Leukocytosis	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	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 (7.14%)	0 (0.00%)	3 (1.62%)
Leukopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)

Lymphopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.25%)	3 (1.62%)
Neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	3 (6.25%)	5 (2.70%)
Neutrophilia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (8.33%)	5 (2.70%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	3 (1.62%)
Cardiac disorders																			
Angina pectoris	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Cardiac failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Sinus tachycardia	1 (16.67%)	1 (16.67%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	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 (9.09%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Ventricular extrasystoles	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Ear and labyrinth disorders																			
Ear congestion	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)

Ear discomfort	0 (0.00%)	0 (0.00%)	1 (2.63%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Hypoacusis	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Tinnitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Endocrine disorders																		
Adrenal insufficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Hyperthyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	2 (1.08%)
Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	2 (18.18%)	0 (0.00%)	2 (14.29%)	0 (0.00%)	5 (2.70%)
Eye disorders																		
Asthenopia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Lacrimation increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Vision blurred	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	2 (1.08%)
Visual impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)

Gastrointestinal disorders																	
Abdominal distension	0 (0.00%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	1 (2.08%)	6 (3.24%)
Abdominal mass	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Abdominal pain	1 (16.67%)	0 (0.00%)	9 (23.68%)	2 (18.18%)	4 (40.00%)	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (50.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	4 (8.33%)	26 (14.05%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	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 (7.14%)	1 (2.08%)	3 (1.62%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	2 (5.26%)	3 (27.27%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	3 (6.25%)	11 (5.95%)
Anal incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Ascites	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	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 (1.08%)
Constipation	1 (16.67%)	2 (33.33%)	7 (18.42%)	0 (0.00%)	0 (0.00%)	3 (50.00%)	3 (60.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	2 (50.00%)	2 (18.18%)	3 (60.00%)	2 (14.29%)	9 (18.75%)	37 (20.00%)
Diarrhoea	1 (16.67%)	0 (0.00%)	10 (26.32%)	5 (45.45%)	5 (50.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	2 (40.00%)	2 (14.29%)	11 (22.92%)	43 (23.24%)
Dry mouth	1 (16.67%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	7 (3.78%)

Dyspepsia	1 (16.67%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	2 (4.17%)	6 (3.24%)
Dysphagia	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	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%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Enteritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Enterovesical 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Flatulence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	2 (1.08%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	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 (2.08%)	3 (1.62%)
Gingival bleeding	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Haematochezia	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Haemorrhoids	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	3 (1.62%)
Intestinal obstruction	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Loose tooth	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)

Mouth ulceration	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Nausea	1 (16.67%)	3 (50.00%)	8 (21.05%)	6 (54.55%)	5 (50.00%)	4 (66.67%)	1 (20.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (25.00%)	4 (36.36%)	1 (20.00%)	4 (28.57%)	16 (33.33%)	56 (30.27%)
Retching	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Stomatitis	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (9.09%)	2 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.0 8%)	5 (2.7 0%)
Tongue disorder	0 (0.00%)	1 (16.67%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Tooth discolouration	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Toothache	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.1 7%)	3 (1.6 2%)
Vomiting	1 (16.67%)	2 (33.33%)	10 (26.32%)	3 (27.27%)	4 (40.00%)	3 (50.00%)	1 (20.00%)	1 (25.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (27.27%)	1 (20.00%)	2 (14.29%)	9 (18.75%)	41 (22.16%)
General disorders and administration site conditions																		
Asthenia	0 (0.00%)	1 (16.67%)	8 (21.05%)	2 (18.18%)	3 (30.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	0 (0.00%)	4 (28.57%)	16 (33.33%)	39 (21.08%)

Axillary pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	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 (1.08%)
Catheter site pruritus	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Chest discomfort	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Chills	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	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 (4.17%)	4 (2.16%)
Decreased activity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Drug withdrawal 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%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Early satiety	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Fatigue	0 (0.00%)	3 (50.00%)	9 (23.68%)	4 (36.36%)	3 (30.00%)	3 (50.00%)	3 (60.00%)	2 (50.00%)	1 (33.33%)	0 (0.00%)	2 (40.00%)	1 (25.00%)	3 (75.00%)	4 (36.36%)	0 (0.00%)	5 (35.71%)	6 (12.50%)	49 (26.49%)
Gait disturbance	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	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 (20.00%)	1 (7.14%)	0 (0.00%)	5 (2.70%)
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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Malaise	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	1 (10.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	5 (2.70%)
Mucosal dryness	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)

Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	3 (6.25%)	7 (3.78%)
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 (33.33%)	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 (0.54%)
Oedema peripheral	1 (16.67%)	0 (0.00%)	4 (10.53%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	2 (40.00%)	1 (7.14%)	2 (4.17%)	15 (8.11%)
Pain	1 (16.67%)	0 (0.00%)	3 (7.89%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	5 (2.70%)
Pyrexia	0 (0.00%)	1 (16.67%)	4 (10.53%)	3 (27.27%)	4 (40.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	5 (10.42%)	20 (10.81%)
Swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	1 (2.08%)	2 (1.08%)
Xerosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Hepatobiliary disorders																		
Cholestasis	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Hyperbilirubinaemia	1 (16.67%)	1 (16.67%)	1 (2.63%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	6 (3.24%)
Hypertransaminasaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	2 (1.08%)
Immune system disorders																		

Seasonal allergy	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Infections and infestations																		
Breast cellulitis	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.5 4%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	7 (14.58%)	8 (4.3 2%)
Device related infection	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Ear infection	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	1 (2.0 8%)	2 (1.0 8%)
Erysipelas	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Fungal infection	0 (0.00%)	0 (0.00%)	1 (2.6 3%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	2 (1.0 8%)
Hepatic infection	1 (16.67%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Infected skin ulcer	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Influenza	1 (16.67%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.1 7%)	3 (1.6 2%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	1 (2.6 3%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	0 (0.00%)	1 (7.14%)	1 (2.0 8%)	5 (2.7 0%)

Oral candidiasis	0 (0.00%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Oral herpes	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Oropharyngeal candidiasis	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Pseudomonas infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Sinusitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	3 (1.62%)
Skin infection	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Tinea versicolour	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	1 (2.63%)	1 (9.09%)	1 (10.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (2.70%)
Urinary tract infection	0 (0.00%)	1 (16.67%)	4 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (10.42%)	13 (7.03%)
Vaginal infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Vulvovaginal candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)

Injury, poisoning and procedural complications																		
Allergic transfusion reaction	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Breast injury	0 (0.00%)	1 (16.67%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Chest injury	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Contusion	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Epicondylitis	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.54%)
Incision site pain	0 (0.00%)	1 (16.67%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Incision site paraesthesia	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.54%)
Ligament sprain	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Muscle strain	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Post procedural	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)

inflammation																		
Rib fracture	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	3 (1.62%)
Skin abrasion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Skin laceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Investigations																		
Alanine aminotransferase increased	1 (16.67%)	0 (0.00%)	6 (15.79%)	3 (27.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	2 (40.00%)	1 (7.14%)	7 (14.58%)	23 (12.43%)
Amylase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	3 (6.25%)	4 (2.16%)
Aspartate aminotransferase increased	0 (0.00%)	0 (0.00%)	5 (13.16%)	3 (27.27%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	1 (20.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	1 (20.00%)	2 (14.29%)	5 (10.42%)	21 (11.35%)
Bilirubin conjugated increased	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	3 (1.62%)
Blood alkaline phosphatase 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)	2 (4.17%)	4 (2.16%)
Blood alkaline phosphatase increased	1 (16.67%)	1 (16.67%)	5 (13.16%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	2 (4.17%)	15 (8.11%)

Blood bilirubin increased	0 (0.00%)	2 (33.33%)	10 (26.32%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (60.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	2 (14.29%)	4 (8.33%)	23 (12.43%)
Blood calcium increased	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Blood chloride 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
Blood cholesterol increased	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Blood creatine increased	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Blood creatinine increased	0 (0.00%)	0 (0.00%)	5 (13.16%)	1 (9.09%)	1 (10.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	3 (6.25%)	13 (7.03%)
Blood glucose increased	0 (0.00%)	1 (16.67%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	3 (1.62%)
Blood lactate dehydrogenase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (14.29%)	3 (6.25%)	6 (3.24%)
Blood magnesium 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	1 (2.08%)	2 (1.08%)
Blood phosphorus 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	1 (2.08%)	2 (1.08%)

Blood phosphorus increased	0 (0.00%)	1 (16.67%)	1 (2.63%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)	2 (4.17%)	7 (3.78%)
Blood sodium 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
Blood thyroid stimulating hormone 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
Blood thyroid stimulating hormone increased	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	3 (1.62%)
Body temperature increased	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Cortisol 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	1 (0.54%)
C-reactive protein increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	3 (6.25%)	4 (2.16%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Gamma-glutamyltransferase increased	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	3 (1.62%)

International normalised ratio increased	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Lipase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	2 (14.29%)	7 (14.58%)	10 (5.41%)
Liver function test increased	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Lymphocyte count 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Monocyte count increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Neutrophil count 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	2 (1.08%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Platelet count increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Protein total 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	2 (4.17%)	3 (1.62%)
Prothrombin time prolonged	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
SARS-CoV-2	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)

test negative																	
Thyroxine free increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Troponin increased	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Urine calcium/creatinine ratio 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (8.33%)	4 (2.16%)
Vitamin D 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	2 (1.08%)
Weight decreased	0 (0.00%)	0 (0.00%)	5 (13.16%)	1 (9.09%)	4 (40.00%)	2 (33.33%)	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 (20.00%)	1 (7.14%)	2 (4.17%)	17 (9.19%)
Weight increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	1 (2.08%)	2 (1.08%)
Metabolism and nutrition disorders																		
Decreased appetite	1 (16.67%)	2 (33.33%)	18 (47.37%)	5 (45.45%)	5 (50.00%)	4 (66.67%)	3 (60.00%)	2 (50.00%)	2 (66.67%)	1 (20.00%)	1 (20.00%)	0 (0.00%)	2 (50.00%)	4 (36.36%)	0 (0.00%)	6 (42.86%)	13 (27.08%)	69 (37.30%)
Dehydration	0 (0.00%)	0 (0.00%)	5 (13.16%)	1 (9.09%)	3 (30.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (7.14%)	0 (0.00%)	13 (7.03%)
Electrolyte imbalance	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Gout	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)

Hyperalbuminaemia	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Hypercalcaemia	1 (16.67%)	0 (0.00%)	9 (23.68%)	2 (18.18%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	1 (25.00%)	3 (100.00%)	1 (20.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	25 (13.51%)
Hyperchloraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.25%)	3 (1.62%)
Hyperglycaemia	0 (0.00%)	1 (16.67%)	4 (10.53%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (18.18%)	1 (20.00%)	0 (0.00%)	4 (8.33%)	15 (8.11%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	1 (2.63%)	1 (9.09%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (60.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	6 (3.24%)
Hyperphosphataemia	2 (33.33%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	4 (2.16%)
Hypoalbuminaemia	0 (0.00%)	3 (50.00%)	2 (5.26%)	1 (9.09%)	1 (10.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (4.17%)	13 (7.03%)
Hypocalcaemia	0 (0.00%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	3 (6.25%)	10 (5.41%)
Hypoglycaemia	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Hypokalaemia	2 (33.33%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (18.18%)	1 (20.00%)	2 (14.29%)	3 (6.25%)	15 (8.11%)
Hypomagnesaemia	0 (0.00%)	2 (33.33%)	3 (7.89%)	2 (18.18%)	4 (40.00%)	1 (16.67%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	3 (60.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	4 (8.33%)	23 (12.43%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	1 (10.00%)	1 (16.67%)	0 (0.00%)	1 (25.00%)	1 (33.33%)	2 (40.00%)	1 (20.00%)	1 (25.00%)	1 (25.00%)	1 (9.09%)	1 (20.00%)	1 (7.14%)	1 (2.08%)	14 (7.57%)

Hypophosphataemia	0 (0.00%)	0 (0.00%)	2 (5.26%)	2 (18.18%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	2 (14.29%)	3 (6.25%)	13 (7.03%)
Type 1 diabetes mellitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Musculoskeletal and connective tissue disorders																		
Arthralgia	0 (0.00%)	0 (0.00%)	6 (15.79%)	2 (18.18%)	1 (10.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	1 (33.33%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	1 (25.00%)	2 (18.18%)	1 (20.00%)	2 (14.29%)	8 (16.67%)	28 (15.14%)
Back pain	0 (0.00%)	0 (0.00%)	5 (13.16%)	2 (18.18%)	2 (20.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (27.27%)	1 (20.00%)	0 (0.00%)	9 (18.75%)	23 (12.43%)
Flank pain	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	2 (14.29%)	0 (0.00%)	5 (2.70%)
Groin pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Muscle spasms	2 (33.33%)	2 (33.33%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	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%)	0 (0.00%)	1 (2.08%)	8 (4.32%)
Muscle tightness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Muscular weakness	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)

Musculoskeletal discomfort	0 (0.00%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Musculoskeletal pain	0 (0.00%)	0 (0.00%)	5 (13.16%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	7 (3.78%)
Myalgia	0 (0.00%)	0 (0.00%)	4 (10.53%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	8 (16.67%)	16 (8.65%)
Neck 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 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	2 (4.17%)	4 (2.16%)
Osteopenia	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	1 (20.00%)	1 (7.14%)	1 (2.08%)	7 (3.78%)
Pain in extremity	0 (0.00%)	0 (0.00%)	3 (7.89%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	6 (12.50%)	14 (7.57%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)																		
Cancer pain	1 (16.67%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	1 (2.08%)	5 (2.70%)
Infected neoplasm	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Metastases to central nervous system	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)

Metastases to soft tissue	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Tumour associated fever	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
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 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	1 (2.08%)	3 (1.62%)
Nervous system disorders																		
Anosmia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Aphasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Balance disorder	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	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 (2.08%)	2 (1.08%)
Depressed level of consciousness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Disturbance in attention	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Dizziness	0 (0.00%)	1 (16.67%)	2 (5.26%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	1 (20.00%)	1 (7.14%)	1 (2.08%)	10 (5.41%)
Dysaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Dysgeusia	0 (0.00%)	2 (33.33%)	15 (39.47%)	3 (27.27%)	3 (30.00%)	2 (33.33%)	1 (20.00%)	3 (75.00%)	2 (66.67%)	2 (40.00%)	2 (40.00%)	1 (25.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	2 (14.29%)	8 (16.67%)	47 (25.41%)

Headache	0 (0.00%)	1 (16.67%)	4 (10.53%)	1 (9.09%)	3 (30.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (18.18%)	0 (0.00%)	5 (35.71%)	6 (12.50%)	23 (12.43%)
Hypoaesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	1 (0.54%)
Hypogeusia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Lethargy	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Memory impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	1 (2.08%)	2 (1.08%)
Neuralgia	0 (0.00%)	0 (0.00%)	3 (7.89%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (4.17%)	5 (2.70%)
Neuropathy peripheral	1 (16.67%)	0 (0.00%)	1 (2.63%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Paraesthesia	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	6 (12.50%)	9 (4.86%)
Parosmia	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	2 (1.08%)
Quadrantanopia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Restless legs 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Sacral radiculopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)

Sciatica	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.0 8%)	2 (1.0 8%)
Seizure	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Sensory disturbance	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.5 4%)
Sinus headache	0 (0.00%)	1 (16.67%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Somnolence	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.0 8%)	2 (1.0 8%)
Taste disorder	1 (16.67%)	1 (16.67%)	1 (2.6 3%)	2 (18.18%)	3 (30.00%)	1 (16.67%)	2 (40.00%)	1 (25.00%)	1 (33.33%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (2.0 8%)	16 (8.65%)
Tremor	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	2 (1.0 8%)
Psychiatric disorders																		
Agitation	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Anxiety	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	4 (8.33%)	8 (4.32%)
Confusional state	0 (0.00%)	0 (0.00%)	2 (5.2 6%)	1 (9.09%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	4 (2.1 6%)
Depression	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	2 (4.17%)	4 (2.1 6%)

Insomnia	0 (0.00%)	1 (16.67%)	3 (7.89%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	1 (2.08%)	7 (3.78%)
Mental status changes	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Sleep disorder	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Renal and urinary disorders																		
Acute kidney injury	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	3 (1.62%)
Azotaemia	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Choluria	0 (0.00%)	0 (0.00%)	1 (2.63%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	2 (1.08%)
Dysuria	0 (0.00%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	4 (2.16%)
Haemoglobinuria	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Ketonuria	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)
Polyuria	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	2 (1.08%)
Renal failure	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	4 (2.16%)
Urinary hesitation	1 (16.67%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.54%)

Urinary retention	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Pelvic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	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 (1.08%)
Respiratory, thoracic and mediastinal disorders																		
Asthmatic crisis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Chronic obstructive pulmonary disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Cough	1 (16.67%)	1 (16.67%)	5 (13.16%)	1 (9.09%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (25.00%)	6 (54.55%)	0 (0.00%)	0 (0.00%)	7 (14.58%)	24 (12.97%)
Dysphonia	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (1.62%)
Dyspnoea	3 (50.00%)	1 (16.67%)	5 (13.16%)	2 (18.18%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	2 (4.17%)	19 (10.27%)
Epistaxis	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	5 (2.70%)

Haemoptysis	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	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 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)
Hiccups	0 (0.00%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	2 (1.08%)
Hyperventilation	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Hypoxia	0 (0.00%)	1 (16.67%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Nasal discharge discolouration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Pleural effusion	1 (16.67%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (2.16%)
Pleuritic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Pneumonitis	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	1 (7.14%)	0 (0.00%)	3 (1.62%)
Productive cough	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (2.08%)	5 (2.70%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)	0 (0.00%)	3 (1.62%)
Pulmonary 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%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)
Rhinitis allergic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (20.00%)	0 (0.00%)	0 (0.00%)	1 (0.54%)

Skin and subcutaneous tissue disorders																		
Alopecia	0 (0.00%)	1 (16.67%)	2 (5.26%)	3 (27.27%)	2 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (50.00%)	1 (9.09%)	0 (0.00%)	2 (14.29%)	14 (29.17%)	28 (15.14%)
Blister	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Dermatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (10.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Dry skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (18.18%)	0 (0.00%)	0 (0.00%)	1 (2.08%)	6 (3.24%)
Erythema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.25%)	3 (1.62%)
Onycholysis	0 (0.00%)	0 (0.00%)	2 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (1.08%)
Onychomadesis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (0.54%)
Palmar-plantar erythrodysaesthesia syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	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 (7.14%)	0 (0.00%)	2 (1.08%)
Pruritus	0 (0.00%)	0 (0.00%)	2 (5.26%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (9.09%)	1 (20.00%)	1 (7.14%)	12 (25.00%)	21 (11.35%)
Rash	0 (0.00%)	0 (0.00%)	3 (7.89%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	1 (20.00%)	0 (0.00%)	4 (8.33%)	11 (5.95%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	1 (2.63%)	0 (0.00%)	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 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (1.08%)

Rash papular	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.09%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Rash pruritic	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.5 4%)
Scab	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Skin lesion	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	3 (1.6 2%)
Skin mass	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	1 (0.5 4%)
Skin ulcer	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.5 4%)
Vascular disorders																		
Deep vein thrombosis	0 (0.00%)	1 (16.67%)	1 (2.6 3%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	2 (1.0 8%)
Haematoma	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	2 (1.0 8%)
Hypertension	0 (0.00%)	0 (0.00%)	1 (2.6 3%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.0 8%)	3 (1.6 2%)
Hypotension	0 (0.00%)	0 (0.00%)	2 (5.2 6%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (14.29%)	3 (6.2 5%)	9 (4.8 6%)
Lymphoedema	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.1 7%)	3 (1.6 2%)
Systolic hypertension	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (7.14%)	0 (0.0 0%)	1 (0.5 4%)

Conclusion:

The study was completed per the protocol. A recommended dose for expansion (RDE) was established for both LGK974 single agent and LGK974 in combination with PDR001. No MTD was established for either regimen.

The overall safety profile of LGK974 as a single agent and LGK974 in combination with PDR001 was characterized and determined acceptable.

Efficacy of LGK974 single agent was limited with no patient achieving an objective response. In the combination arm, anti-tumor activity was observed.

Date of Clinical Trial Report

18-Mar-2025