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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

NIZ985 and spartalizumab (PDR001)

Trial Indication(s)

Metastatic cancers

Protocol Number

CNIZ985X2102J

Protocol Title

A Phase 1 Study of Subcutaneous Recombinant Human NIZ985 ((hetIL-15) (IL15/sIL-15Ra)) alone and in combination with PDR001 in adults with metastatic cancers

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1 (NIZ985) and Phase 3 (spartalizumab)

Study Start/End Dates

Study Start Date: May 08, 2017 (Actual)
Primary Completion Date: March 07, 2022 (Actual)
Study Completion Date: March 07, 2022 (Actual)

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Reason for Termination (If applicable)

This study decided to halt further recruitment of patients based on a business decision due to limitations of global product development using a HEK-derived product. This decision was not due to any serious safety concerns.

Study Design/Methodology

This was a Phase I/Ib, multi-center, open-label study starting with dose escalation to determine the Maximum Tolerated Dose(s) (MTD(s)) and/or Recommended Dose(s) for Expansion (RDE(s)) of NIZ985 when administered alone (single agent arm) and in combination with PDR001 400 mg every 4 weeks (Q4W) (combination arm).

After the identification of MTDs and/or RDEs of NIZ985, a dose expansion part could be opened with one of the two NIZ985 schedules (three times a week or weekly) for the single agent arm and with one or both NIZ985 schedules for the combination arm, to further characterize the safety, pharmacokinetics (PK), and preliminary activity of the monotherapy and the combination. The expansion part for the combination arm consisted of 2 groups, patients with tumor types that are historically resistant to anti-PD-1 therapy and patients with tumor types that are historically sensitive to anti-PD-1 therapy (e.g. NSCLC, melanoma, and bladder). Patients were considered to be sensitive to an anti-PD-1 therapy if such therapy had been approved by regulatory authorities for specific indications (e.g., non-small cell lung cancer, melanoma, and bladder cancer). Resistance to an anti-PD-1 agent was defined as a lack of response to the treatment with anti-PD-1 agents based on published studies or if these agents are still being investigated in patients with specific tumor types.

For the single agent (SA) arm, the expansion part was not opened. For the combination arm, the expansion part was opened only with one out of two dosing schedules investigated for NIZ985.

Centers

United States(7)

Objectives:

The primary objectives of the trial were:

- To characterize the safety and tolerability of NIZ985 alone and in combination with PDR001
- To identify MTD(s) and/or RDE(s) of NIZ985 alone and in combination with PDR001

The secondary objectives of the trial were:

- To evaluate the preliminary anti-tumor activity of NIZ985 alone and in combination with PDR001
- To characterize the PK profile of NIZ985 when administered alone and of NIZ985 and PDR001 when administered in combination
- To assess immunogenicity of NIZ985 alone and in combination with PDR001

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

Two dosing schedules were investigated for NIZ985: the original three times a week (TIW) schedule of six subcutaneous (SC) injections in total (3 injections per week, 2 weeks on and 2 weeks off) during each 28-day treatment cycle; and the alternate weekly schedule of three SC injections in total (1 injection per week, 3 weeks on and 1 week off) during each 28-day treatment cycle.

NIZ985 was administered alone (single agent arm) and in combination with PDR001 (combination arm). PDR001 was administered at a fixed dose of 400 mg Q4W.

Single Agent arm

- TIW dosing schedule: NIZ985 0.25 µg/kg, 0.5 µg/kg, 1 µg/kg, 2 µg/kg and 4 µg/kg
- Weekly dosing schedule: NIZ985 2 µg/kg, 4 µg/kg, 6 µg/kg and 10 µg/kg

Combination arm

- TIW dosing schedule: NIZ985 1 µg/kg TIW + PDR001 400 mg Q4W

– Weekly dosing schedule: NIZ985 2 µg/kg weekly + PDR001 400 mg Q4W and NIZ985 4 µg/kg weekly + PDR001 400 mg Q4W

Patients could continue to receive NIZ985 as single agent or in combination with PDR001 until disease progression or until meeting a stopping rule as defined in the protocol.

Statistical Methods

Efficacy: All efficacy analyses (Best Overall Response (BOR), Overall Response Rate (ORR), Disease Control rate (DCR), Progression-Free Survival (PFS), and Duration of Response (DOR)) were based on the Full Analysis Set (FAS) unless otherwise specified. The FAS included all patients who received at least 1 full or partial dose of study treatment. Kaplan-Meier plots for PFS per RECIST v1.1 were presented limited to the groups (by dose level or by anti-PD-1 disease status) of size ≥ 10 patients with estimable median PFS. DOR was estimated only if there were ≥ 10 responders per RECIST v1.1 and irRC within the same group.

Safety: The Safety Set was used for all safety analyses except for the Dose Limiting Toxicities (DLTs). The Safety Set included all patients who received at least 1 dose of study drug and had at least 1 valid post-baseline safety assessment. DLTs were summarized based on the dose-determining set which consisted of all patients from the Safety Set in the dose escalation part who either met the minimum exposure criterion or experienced a DLT during Cycle 1 for the single agent arm and during Cycles 1 and 2 for the combination arm.

Pharmacokinetics and immunogenicity: All PK analyses were based on the PK Analysis Set (PAS), which consisted of all patients who provided an evaluable PK profile for either of the dosing schedules. PK parameters were determined by non-compartmental method(s) using the concentration listing of NIZ985 and PDR001. PK parameters were derived and reported when feasible.

Patient anti-drug antibody (ADA) status was summarized based on the Immunogenicity Incidence Set, which consisted of all patients in the Immunogenicity Prevalence Set with a determinant baseline immunogenicity sample and at least 1 determinant post-baseline immunogenicity sample.

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Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Histologically confirmed solid tumor malignancy that is metastatic or unresectable and have progressed on at least 1 prior therapy and for whom standard curative or palliative measures do not exist or are associated with minimal subject survival benefit.

Evaluable or measurable disease, defined as by Response Evaluation Criteria in Solid Tumors (RECIST).

2. Recovered to ≤ grade 1 NCI CTCAE version 4.0 from toxicity of prior chemotherapy or biologic therapy administered more than 4 weeks earlier.

3. Subjects on bisphosphonates for any cancer or on hormone therapy for prostate cancer may continue this therapy. However, subjects with prostate cancer must have confirmed metastatic disease that has progressed despite hormonal therapy producing castrate levels of testosterone.

4. Age ≥18 years.

5. ECOG performance status ≤1 (Karnofsky ≥70%).

6. Normal organ and marrow function:

- leukocytes ≥3,000/mcL
- absolute neutrophil count (ANC) ≥1,500/mcL
- platelets ≥100,000/mcL
- total bilirubin within normal institutional limits
- AST/ALT ≤2.5 × ULN
- creatinine <1.5 × institutional ULN OR
- creatinine clearance ≥60 mL/min/1.73 m2 for subjects with serum creatinine levels >1.5 × higher than ULN.

7. DLCO/VA and FEV1 ≥ 50% of predicted on PFTs.

8. Subjects with inactive central nervous system (CNS) metastasis are eligible..

9. Women of child-bearing potential and men must agree to use adequate contraception prior to study entry, during the treatment portion of the study and for 4 months after completion of hetIL-15 administration.

10. Able to provide written informed consent.

11. Life expectancy > 3 months.

Exclusion Criteria:

1. Prior IL-15 treatment or cytotoxic therapy, immunotherapy, radiotherapy, major surgery, antitumor vaccines or monoclonal antibodies in the 4 weeks prior or for checkpoint inhibitors such as anti-CTLA-4 or anti PD1/PD-L1 or nitrosoureas or mitomycin C for 6 weeks prior to C1D1.
2. Primary brain cancers or active CNS metastases should be excluded from this clinical trial
3. History of allergic reactions attributed to compounds of similar chemical or biologic composition to hetIL-15.
4. Concurrent anticancer therapy (including other investigational agents) with the exception of hormone therapy for prostate cancer.
5. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, cognitive impairment, active substance abuse, or psychiatric illness/social situations that, in the view of the Investigator, would preclude safe treatment or the ability to give informed consent and limit compliance with study requirements.
6. HIV positive patients.
7. Positive hepatitis B or C serology.
8. History of severe asthma or absolute requirement for chronic inhaled corticosteroid medications.
9. History of autoimmune disease, with the exception of an autoimmune event associated with prior ipilimumab (anti-CTLA-4) therapy that has been completely resolved for more than 4 weeks prior to C1D1.

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Participant Flow Table

Overall Study

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	NIZ985 1 µg/kg TIW + PDR001 400 mg	NIZ985 2 µg/kg Weekly + PDR001 400 mg	NIZ985 4 µg/kg Weekly + PDR001 400 mg	NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant	NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive	Total
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy	
Started	1	2	6	3	2	3	3	3	4	11	4	5	25	11	83
Completed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Not Completed	1	2	6	3	2	3	3	3	4	11	4	5	25	11	83
Adverse Event	0	1	0	1	1	1	0	1	0	2	0	2	0	0	9
Other	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Physician Decision	0	0	0	0	1	0	0	1	1	0	1	0	2	0	6

Progressive disease	1	1	5	2	0	1	2	1	3	8	3	2	20	9	58
Withdrawal by Subject	0	0	1	0	0	1	0	0	0	1	0	1	0	0	4
Death	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2
Study terminated by sponsor	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Subject decision	0	0	0	0	0	0	0	0	0	0	0	0	2	0	2

Baseline Characteristics

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**	**Total**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with	Dose escalation part, NIZ985 4 µg/kg weekly in combination with	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors	

											PDR001	PDR001	resistant to anti-PD-1 therapy	sensitive to anti-PD-1 therapy	
Number of Participants [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11	83
Age Continuous (units: years) Analysis Population Type: Mean ± Standard Deviation															
	50.0	61.5±3.54	53.7±9.95	59.3±11.85	62.5±6.36	71.3±12.50	64.7±1.53	68.7±9.50	66.5±9.00	59.5±12.99	62.8±9.84	66.2±6.72	60.0±13.64	59.1±18.07	61.0±12.50
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)															
Female	0	1	2	2	1	2	1	0	1	4	1	1	16	4	36
Male	1	1	4	1	1	1	2	3	3	7	3	4	9	7	47
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)															
White	1	2	5	2	2	3	3	2	3	11	4	5	22	9	74
Asian	0	0	0	0	0	0	0	1	0	0	0	0	2	1	4
Black or African American	0	0	1	0	0	0	0	0	0	0	0	0	1	1	3

Not reported	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1
Unknown	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1

Primary Outcome Result(s)

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

Description: Number of participants with AEs and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. The on-treatment period is defined from the day of first administration of study treatment up to 30 days after the date of its last administration. Grades to characterize the severity of the AEs were based on the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. For CTCAE, Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe; Grade 4 = life threatening; Grade 5 (death).

Time Frame: From first dose of study treatment up to 30 days after last dose, with a maximum duration of 2.1 years for NIZ985 single agent arm and 2.9 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**All NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in	Dose escalation part, NIZ985 2 µg/kg weekly in combinati	Dose escalation part, NIZ985 4 µg/kg weekly in combinati

										combinati on with PDR001	on with PDR001	on with PDR001
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	47	4	5
Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
AEs	1 (100%)	2 (100%)	6 (100%)	3 (100%)	2 (100%)	3 (100%)	3 (100%)	3 (100%)	4 (100%)	47 (100%)	4 (100%)	5 (100%)
Treatment-related AEs	1 (100%)	2 (100%)	6 (100%)	3 (100%)	2 (100%)	3 (100%)	3 (100%)	3 (100%)	4 (100%)	46 (97.87%)	4 (100%)	5 (100%)
AEs with grade ≥ 3	0 (%)	1 (50%)	2 (33.33%)	1 (33.33%)	2 (100%)	3 (100%)	1 (33.33%)	2 (66.67%)	4 (100%)	25 (53.19%)	2 (50%)	2 (40%)
Treatment-related AEs with grade ≥ 3	0 (%)	1 (50%)	1 (16.67%)	1 (33.33%)	2 (100%)	0 (%)	1 (33.33%)	0 (%)	1 (25%)	8 (17.02%)	0 (%)	1 (20%)
SAEs	0 (%)	1 (50%)	1 (16.67%)	2 (66.67%)	1 (50%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	4 (100%)	18 (38.3%)	3 (75%)	1 (20%)
Treatment-related SAEs	0 (%)	0 (%)	0 (%)	2 (66.67%)	1 (50%)	0 (%)	0 (%)	0 (%)	1 (25%)	2 (4.26%)	0 (%)	0 (%)
Fatal SAEs	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (33.33%)	0 (%)	1 (33.33%)	0 (%)	3 (6.38%)	0 (%)	0 (%)

AEs leading to discontinuation	0 (%)	1 (50%)	0 (%)	1 (33.33%)	1 (50%)	1 (33.33%)	0 (%)	1 (33.33%)	0 (%)	1 (2.13%)	1 (25%)	2 (40%)
Treatment-related AEs leading to discontinuation	0 (%)	0 (%)	0 (%)	1 (33.33%)	1 (50%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (20%)
AEs leading to dose adjustment/interruption	0 (%)	0 (%)	0 (%)	0 (%)	2 (100%)	1 (33.33%)	0 (%)	1 (33.33%)	4 (100%)	16 (34.04%)	1 (25%)	3 (60%)
AEs requiring additional therapy	0 (%)	0 (%)	3 (50%)	0 (%)	2 (100%)	3 (100%)	3 (100%)	3 (100%)	4 (100%)	46 (97.87%)	3 (75%)	5 (100%)
Injection site reaction	1 (100%)	2 (100%)	6 (100%)	3 (100%)	2 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (75%)	46 (97.87%)	4 (100%)	5 (100%)
Hypersensitivity or Infusion reaction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	7 (14.89%)	0 (%)	1 (20%)
Potential cytokine release syndrome	0 (%)	0 (%)	0 (%)	0 (%)	1 (50%)	1 (33.33%)	0 (%)	0 (%)	1 (25%)	1 (2.13%)	0 (%)	0 (%)

Number of participants with Dose-Limiting Toxicities (DLTs) (Dose escalation only)

Description: Dose limiting toxicity is defined as Grade 3 or 4 AEs assessed as related to NIZ985 or PDR001 or the combination that occur during the first 28 days (Cycle 1) of treatment with NIZ985 monotherapy or the first 56 days (first 2 cycles) of treatment with NIZ985 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 (single agent arm) and 56 days (combination arm)

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	NIZ985 1 µg/kg TIW +	NIZ985 2 µg/kg Weekly +	NIZ985 4 µg/kg Weekly +

										PDR001 400 mg	PDR001 400 mg	PDR001 400 mg
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Number of Participants Analyzed [units: participants]	1	1	6	3	2	3	3	3	3	7	3	3
Number of participants with Dose-Limiting Toxicities (DLTs) (Dose escalation only) (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Number of participants with dose reductions and dose interruptions of NIZ985

Description Number of participants with at least one dose reduction of NIZ985 and number of participants with at least one dose interruption of NIZ985.

Time Frame From first dose of study treatment up to last dose, with a maximum duration of 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	NIZ985 1 µg/kg TIW + PDR001 400 mg	NIZ985 2 µg/kg Weekly + PDR001 400 mg	NIZ985 4 µg/kg Weekly + PDR001 400 mg	NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant	NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Number of participants with	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**

dose reductions and dose interruptions of NIZ985 (units: participants)	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**
At least one dose reduction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (50%)	1 (9.09%)	0 (%)	1 (20%)	0 (%)	0 (%)
At least one dose interruption	0 (%)	0 (%)	2 (33.33%)	0 (%)	2 (100%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (25%)	7 (63.64%)	1 (25%)	1 (20%)	8 (32%)	7 (63.64%)

Number of participants with dose reductions and dose interruptions of PDR001

Description: Number of participants with at least one dose reduction of PDR001 and number of participants with at least one dose interruption of PDR001.

Time Frame: From first dose of study treatment up to last dose, with a maximum duration of 2.8 years

	NIZ985 1 µg/kg TIW + PDR001 400 mg	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy

Number of Participants Analyzed [units: participants]	11	4	5	25	11
Number of participants with dose reductions and dose interruptions of PDR001 (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
At least one dose reduction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
At least one dose interruption	1 (9.09%)	0 (%)	1 (20%)	1 (4%)	0 (%)

Dose intensity of NIZ985

Description: Dose intensity of NIZ985 was calculated as actual cumulative dose in micrograms divided by duration of exposure in weeks.

Time Frame: From first dose of study treatment up to last dose, with a maximum duration of 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-

													PD-1 therapy	PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Dose intensity of NIZ985 (units: µg/week)	**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)**
	36.30 (36.30 to 36.30)	43.60 (34.42 to 52.78)	144.55 (142.30 to 162.70)	238.53 (229.81 to 253.58)	446.65 (314.72 to 578.57)	124.46 (36.00 to 158.40)	300.70 (241.03 to 373.69)	418.71 (321.00 to 507.00)	424.13 (365.18 to 562.13)	103.74 (77.7 to 151.1)	152.88 (125.0 to 189.1)	277.91 (175.5 to 303.9)	103.65 (38.5 to 167.4)	108.51 (60.1 to 129.1)

Dose intensity of PDR001

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

Time Frame: From first dose of study treatment up to last dose, with a maximum duration of 2.8 years

	NIZ985 1 µg/kg TIW + PDR001 400 mg	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy

Number of Participants Analyzed [units: participants]	11	4	5	25	11
Dose intensity of PDR001 (units: mg/week)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	100.00 (93.6 to 100.0)	99.12 (96.9 to 100.0)	100.00 (87.5 to 100.0)	100.00 (50.0 to 103.7)	100.00 (74.3 to 107.7)

Secondary Outcome Result(s)

Best Overall Response (BOR) per RECIST v1.1

Description: BOR is defined as the best response recorded from the start of the treatment until disease progression/recurrence based on local investigator assessment per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1. 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 diameters of all target lesions, taking as reference the baseline sum of diameters; PD= At least a 20% increase in the sum of diameters of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition, the sum must also demonstrate an absolute increase of at least 5 mm; SD= Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progression.

Time Frame: From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25	Dose escalation part, NIZ985 0.5	Dose escalation part, NIZ985	Dose escalation part, NIZ985	Dose escalation part, NIZ985	Dose escalation part, NIZ985	Dose escalation part, NIZ985	Dose escalation part, NIZ985	Dose escalation part, NIZ985	Dose escalation part, NIZ985 1 µg/kg	Dose escalation part, NIZ985 2 µg/kg	Dose escalation part, NIZ985 4 µg/kg	Dose expansion part, NIZ985 1 µg/kg	Dose expansion part, NIZ985 1 µg/kg

	µg/kg TIW	µg/kg TIW	1 µg/kg TIW	2 µg/kg TIW	4 µg/kg TIW	2 µg/kg weekly	4 µg/kg weekly	6 µg/kg weekly	10 µg/kg weekly	TIW in combination with PDR001	weekly in combination with PDR001	weekly in combination with PDR001	TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Best Overall Response (BOR) per RECIST v1.1 (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Complete Response (CR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Partial Response (PR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (9.09%)	1 (25%)	0 (%)	0 (%)	1 (9.09%)
Stable Disease (SD)	1 (100%)	0 (%)	1 (16.67%)	1 (33.33%)	0 (%)	2 (66.67%)	2 (66.67%)	0 (%)	1 (25%)	4 (36.36%)	1 (25%)	2 (40%)	5 (20%)	4 (36.36%)

Progressive Disease (PD)	0 (%)	1 (50%)	4 (66.67%)	2 (66.67%)	1 (50%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (25%)	6 (54.55%)	1 (25%)	2 (40%)	16 (64%)	5 (45.45%)
Unknown	0 (%)	1 (50%)	1 (16.67%)	0 (%)	1 (50%)	0 (%)	0 (%)	2 (66.67%)	2 (50%)	0 (%)	1 (25%)	1 (20%)	4 (16%)	1 (9.09%)

Overall Response Rate (ORR) per RECIST v1.1

Description	ORR is defined as the percentage of participants with a best overall response of CR or PR based on local investigator assessment per RECIST v1.1. 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	From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-

													PD-1 therapy	PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
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)**
	0 (0 to 97.5)	0 (0 to 84.2)	0 (0 to 45.9)	0 (0 to 70.8)	0 (0 to 84.2)	0 (0 to 70.8)	0 (0 to 70.8)	0 (0 to 70.8)	0 (0 to 60.2)	9.1 (0.2 to 41.3)	25.0 (0.6 to 80.6)	0 (0 to 52.2)	0 (0 to 13.7)	9.1 (0.2 to 41.3)

Disease Control Rate (DCR) per RECIST v1.1

Description	DCR is defined as the percentage of participants with a best overall response of CR, PR or SD based on local investigator assessment per RECIST v1.1. 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; SD= Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progression.
Time Frame	From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	NIZ985 1 µg/kg TIW + PDR00 1 400 mg	NIZ985 2 µg/kg Weekly + PDR00 1 400 mg	NIZ985 4 µg/kg Weekly + PDR00 1 400 mg	NIZ985 1 µg/kg TIW + PDR00 1 400 mg - Resistant	NIZ985 1 µg/kg TIW + PDR00 1 400 mg - Sensitive
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Disease Control Rate (DCR) per RECIST v1.1 (units: percentage of	**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)**

participants)													
	100 (2.5 to 100)	0 (0 to 84.2)	16.7 (0.4 to 64.1)	33.3 (0.8 to 90.6)	0 (0 to 84.2)	66.7 (9.4 to 99.2)	66.7 (9.4 to 99.2)	0 (0 to 70.8)	25.0 (0.6 to 80.6)	45.5 (16.7 to 76.6)	50.0 (6.8 to 93.2)	40.0 (5.3 to 85.3)	20.0 (6.8 to 40.7)	45.5 (16.7 to 76.6)

Duration of Response (DOR) per RECIST v1.1

Description: DOR is defined as the time between the date of first documented response (CR or PR) and the date of first documented progression or death due to underlying cancer. DOR only applies to patients for whom best overall response is CR or PR per RECIST v1.1. DOR was estimated only if there were ≥ 10 responders within the same group.

Time Frame: From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of	0	0	0	0	0	0	0	0	0	1	1	0	0	1

Participants Analyzed [units: participants]														
Duration of Response (DOR) per RECIST v1.1 (units: months)	**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)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
										NA (NA to NA)[1]	NA (NA to NA)[1]			NA (NA to NA)[1]

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

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

Description	PFS is defined as the time from the date of start of treatment to the date of the first documented disease progression (PD per RECIST v1.1) or death due to any cause. If a patient had not had an event, PFS was censored at the date of last adequate tumor assessment. PFS was estimated using the Kaplan-Meier Method in the groups of size ≥ 10 patients. Only combination arm cohorts (escalation and expansion disease groups) with NIZ985 dose level of 1 µg/kg TIW qualified this criterion.
Time Frame	From first dose of study treatment up to last dose, with a maximum duration of 2.8 years

	NIZ985 1 µg/kg TIW + PDR001 400 mg	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy

Number of Participants Analyzed [units: participants]	11	25	11
Progression-Free Survival (PFS) per RECIST v1.1 (units: months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	1.9 (1.1 to NA)[1]	1.6 (1.4 to 1.8)	1.9 (1.6 to 3.5)

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

Best Overall Response (BOR) per irRC

Description: BOR is defined as the best response recorded from the start of the treatment until disease progression/recurrence based on local investigator assessment per Immune-related Response Criteria (irRC). 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; irPD= At least a 20% increase in the sum of diameters of all measured target lesions including new measurable lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition, the sum must also demonstrate an absolute increase of at least 5 mm; irSD= Neither sufficient shrinkage to qualify for irPR or irCR nor an increase in lesions which would qualify for irPD.

Time Frame: From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR00 1 400 mg**	**NIZ985 2 µg/kg Weekly + PDR00 1 400 mg**	**NIZ985 4 µg/kg Weekly + PDR00 1 400 mg**	**NIZ985 1 µg/kg TIW + PDR00 1 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR00 1 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combina	Dose escalation part, NIZ985 4 µg/kg weekly in combina	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001

										tion with PDR001	tion with PDR001	in tumors resistant to anti-PD-1 therapy	in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Best Overall Response (BOR) per irRC (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Complete Response (irCR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
Partial Response (irPR)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	2 (18.18%)	1 (25%)	0 (%)	0 (%)	1 (9.09%)
Stable Disease (irSD)	0 (%)	0 (%)	1 (16.67%)	1 (33.33%)	0 (%)	2 (66.67%)	2 (66.67%)	0 (%)	1 (25%)	4 (36.36%)	1 (25%)	3 (60%)	5 (20%)	5 (45.45%)

Progressive Disease (irPD)	0 (%)	1 (50%)	4 (66.67%)	2 (66.67%)	1 (50%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (25%)	4 (36.36%)	1 (25%)	1 (20%)	15 (60%)	4 (36.36%)
Unknown	1 (100%)	1 (50%)	1 (16.67%)	0 (%)	1 (50%)	0 (%)	0 (%)	2 (66.67%)	2 (50%)	1 (9.09%)	1 (25%)	1 (20%)	5 (20%)	1 (9.09%)

Overall Response Rate (ORR) per irRC

Description: ORR is defined as the percentage of participants with a best overall response of irCR or irPR based on local investigator assessment per irRC. 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: From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-

													PD-1 therapy	PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Overall Response Rate (ORR) per irRC (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)**
	0 (0 to 97.5)	0 (0 to 84.2)	0 (0 to 45.9)	0 (0 to 70.8)	0 (0 to 84.2)	0 (0 to 70.8)	0 (0 to 70.8)	0 (0 to 70.8)	0 (0 to 60.2)	18.2 (2.3 to 51.8)	25.0 (0.6 to 80.6)	0 (0 to 52.2)	0 (0 to 13.7)	9.1 (0.2 to 41.3)

Disease Control Rate (DCR) per irRC

Description	DCR is defined as the percentage of participants with a best overall response of irCR, irPR or irSD based on local investigator assessment per irRC. 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; irSD= Neither sufficient shrinkage to qualify for irPR or irCR nor an increase in lesions which would qualify for irPD.
Time Frame	From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	NIZ985 1 µg/kg TIW + PDR00 1 400 mg	NIZ985 2 µg/kg Weekly + PDR00 1 400 mg	NIZ985 4 µg/kg Weekly + PDR00 1 400 mg	NIZ985 1 µg/kg TIW + PDR00 1 400 mg - Resistant	NIZ985 1 µg/kg TIW + PDR00 1 400 mg - Sensitive
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	1	2	6	3	2	3	3	3	4	11	4	5	25	11
Disease Control Rate (DCR) per irRC (units: percentage of	**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)**

participants)														
	0 (0 to 97.5)	0 (0 to 84.2)	16.7 (0.4 to 64.1)	33.3 (0.8 to 90.6)	0 (0 to 84.2)	66.7 (9.4 to 99.2)	66.7 (9.4 to 99.2)	0 (0 to 70.8)	25.0 (0.6 to 80.6)	54.5 (23.4 to 83.3)	50.0 (6.8 to 93.2)	60.0 (14.7 to 94.7)	20.0 (6.8 to 40.7)	54.5 (23.4 to 83.3)

Duration of Response (DOR) per irRC

Description: DOR is defined as the time between the date of first documented response (irCR or irPR) and the date of first documented progression or death due to underlying cancer. DOR only applies to patients for whom best overall response is irCR or irPR per irRC. DOR was estimated only if there were ≥ 10 responders within the same group.

Time Frame: From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of	0	0	0	0	0	0	0	0	0	2	1	0	0	1

Participants Analyzed [units: participants]														
Duration of Response (DOR) per irRC (units: months)	**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)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
										NA (NA to NA)[1]	NA (NA to NA)[1]			NA (NA to NA)[1]

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

Progression-Free Survival (PFS) per irRC

Description	PFS is defined as the time from the date of start of treatment to the date of the first documented disease progression (irPD per irRC) or death due to any cause. If a patient had not had an event, PFS was censored at the date of last adequate tumor assessment. PFS was estimated using the Kaplan-Meier Method in the groups of size ≥ 10 patients. Only combination arm cohorts (escalation and expansion disease groups) with NIZ985 dose level of 1 µg/kg TIW qualified this criterion.
Time Frame	From first dose of study treatment up to last dose, with a maximum duration of 2.8 years

	NIZ985 1 µg/kg TIW + PDR001 400 mg	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant**	**NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive**
Arm/Group Description	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy

Number of Participants Analyzed [units: participants]	11	25	11
Progression-Free Survival (PFS) per irRC (units: months)	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**	**Median (95% Confidence Interval)**
	5.4 (1.1 to NA)[1]	1.6 (1.5 to 1.9)	3.5 (1.6 to 5.4)

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

Maximum observed serum concentration (Cmax) of NIZ985

Description: Pharmacokinetic (PK) parameters were calculated based on NIZ985 serum concentrations by using non-compartmental methods.

Time Frame: pre-dose, 1, 4, 8, 24 and 48 hours post-dose on Cycle 1 Day 1 (all cohorts), Cycle 1 Day 8 (NIZ985 TIW dosing schedule) and Cycle 1 Day 15 (NIZ985 weekly dosing schedule)

	NIZ985 0.25 µg/kg TIW	**NIZ985 0.5 µg/kg TIW**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**All NIZ985 1 µg/kg TIW + PDR001 400 mg**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Number of Participants Analyzed [units: participants]	0	0	6	3	2	3	3	3	4	47	4	5

Maximum observed serum concentration (Cmax) of NIZ985 (units: pg/mL)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)	Geometric Mean (Geometric Coefficient of Variation)
Cycle 1 Day 1 (n=0,0,6,3,2,2,3,3, 4,47,4,5)			96.1 (33.7%)	122 (51.6%)	233 (123.7%)	133 (35.4%)	311 (103.1%)	554 (19.1%)	832 (167.9%)	122 (87.6%)	203 (75.2%)	418 (97.6%)
Cycle 1 Day 8 (n=0,0,5,3,1,0,0,0, 0,40,0,0)			69.4 (3.2%)	81.2	53.9					115 (113.4%)		
Cycle 1 Day 15 (n=0,0,0,0,0,1,3,3, 3,0,4,4)						115	155 (60.2%)	426 (34.8%)	430 (93.8%)		130 (97.6%)	88.8 (28.6%)

Time to reach maximum serum concentration (Tmax) of NIZ985

Description	PK parameters were calculated based on NIZ985 serum concentrations by using non-compartmental methods. Actual recorded sampling times were considered for the calculations.
Time Frame	pre-dose, 1, 4, 8, 24 and 48 hours post-dose on Cycle 1 Day 1 (all cohorts), Cycle 1 Day 8 (NIZ985 TIW dosing schedule) and Cycle 1 Day 15 (NIZ985 weekly dosing schedule)

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	All NIZ985 1 µg/kg TIW + PDR001 400 mg	NIZ985 2 µg/kg Weekly + PDR001 400 mg	NIZ985 4 µg/kg Weekly + PDR001 400 mg
Arm/Group Description	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation part,	Dose escalation and dose	Dose escalation part,	Dose escalation part,

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg weekly	NIZ985 4 µg/kg weekly	NIZ985 6 µg/kg weekly	NIZ985 10 µg/kg weekly	expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	NIZ985 2 µg/kg weekly in combination with PDR001	NIZ985 4 µg/kg weekly in combination with PDR001
Number of Participants Analyzed [units: participants]	0	0	6	3	2	3	3	3	4	47	4	5
Time to reach maximum serum concentration (Tmax) of NIZ985 (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)**	**Median (Full Range)**	**Median (Full Range)**
Cycle 1 Day 1 (n=0,0,6,3,2,2,3,3,4,47, 4,5)			18 (0 to 27.4)	23 (12 to 23.9)	27.7 (7.17 to 48.3)	13.3 (4 to 22.7)	21.6 (4 to 23.5)	7.67 (7.62 to 25)	15.4 (4.07 to 24)	4.07 (0 to 49.1)	14.9 (4.13 to 24.1)	7.57 (4.02 to 24.1)
Cycle 1 Day 8 (n=0,0,5,3,1,0,0,0,0,40, 0,0)			4 (0 to 8.12)	2 (1.85 to 8)	24.6 (24.6 to 24.6)					0 (0 to 23.6)		
Cycle 1 Day 15 (n=0,0,0,0,0,1,3,3,3,0,4, 4)						8 (8 to 8)	8 (7.68 to 23.1)	8 (7.05 to 24.8)	7.85 (4.05 to 23.8)		5.79 (4 to 7.73)	15.4 (7.57 to 24.6)

Area under the serum concentration-time curve from time zero to 48 hours post-dose (AUC48) of NIZ985

Description: PK parameters were calculated based on NIZ985 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.

Time Frame: pre-dose, 1, 4, 8, 24 and 48 hours post-dose on Cycle 1 Day 1 (all cohorts), Cycle 1 Day 8 (NIZ985 TIW dosing schedule) and Cycle 1 Day 15 (NIZ985 weekly dosing schedule)

NIZ985 0.25	**NIZ985 0.5**	**NIZ985 1 µg/kg TIW**	**NIZ985 2 µg/kg TIW**	**NIZ985 4 µg/kg TIW**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly**	**NIZ985 6 µg/kg Weekly**	**NIZ985 10 µg/kg Weekly**	**All NIZ985 1 µg/kg**	**NIZ985 2 µg/kg Weekly**	**NIZ985 4 µg/kg Weekly +**

	µg/kg TIW	µg/kg TIW								TIW + PDR001 400 mg	+ PDR001 400 mg	PDR001 400 mg
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Number of Participants Analyzed [units: participants]	0	0	6	3	2	3	3	3	4	47	4	5
Area under the serum concentration-time curve from time zero to 48 hours post-dose (AUC48) of NIZ985 (units: h*pg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=0,0,3,0,2,2,3,3,3,18,4,5)			2070 (105.3%)		6270 (107.9%)	2400 (220.6%)	9000 (91.1%)	17100 (99.9%)	34800 (144.7%)	2210 (183.2%)	5030 (71.9%)	13200 (81.0%)
Cycle 1 Day 8 (n=0,0,0,0,0,0,0,0,0,21,0,0)										2120 (674.7%)		
Cycle 1 Day 15 (n=0,0,0,0,0,1,1,2,0,0,1,2)						2150	2430	9570 (5.7%)			1720	1100 (76.1%)

Area under the serum concentration-time curve from time zero to 168 hours post-dose (AUC168) of NIZ985

Description: PK parameters were calculated based on NIZ985 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.

Time Frame: pre-dose, 1, 4, 8, 24, 48 and 168 hours post-dose on Cycle 1 Day 1 (Weekly schedule for single agent arm and combination arm and TIW schedule for combination arm) and Cycle 1 Day 8 (TIW schedule for combination arm)

	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	All NIZ985 1 µg/kg TIW + PDR001 400 mg	NIZ985 2 µg/kg Weekly + PDR001 400 mg	NIZ985 4 µg/kg Weekly + PDR001 400 mg
Arm/Group Description	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Number of Participants Analyzed [units: participants]	2	2	2	1	3	2	4
Area under the serum concentration-time curve from time zero to 168 hours post-dose (AUC168) of NIZ985 (units: h*pg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=2,2,2,1,0,2,4)	2830 (325.7%)	17900 (9.2%)	25300 (3.2%)	84000		7170 (135.9%)	23900 (62.1%)
Cycle 1 Day 8 (n=0,0,0,0,3,0,0)					90000 (71.5%)		

Maximum observed serum concentration (Cmax) of PDR001

Description: PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. For PDR001, PK parameters were summarized only for the TIW schedule for the combination arm.

Time Frame: From pre-dose up to 672 hours post dose on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of each cycle was 28 days.

	All NIZ985 1 µg/kg TIW + PDR001 400 mg
Arm/Group Description	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001
Number of Participants Analyzed [units: participants]	47
Maximum observed serum concentration (Cmax) of PDR001 (units: µg/mL)	**Geometric Mean (Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=47)	76.4 (35.6%)
Cycle 3 Day 1 (n=23)	130 (20.8%)

Time to reach maximum serum concentration (Tmax) of PDR001

Description: PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. Actual recorded sampling times were considered for the calculations. For PDR001, PK parameters were summarized only for the TIW schedule for the combination arm.

Time Frame: From pre-dose up to 672 hours post dose on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of each cycle was 28 days.

	All NIZ985 1 µg/kg TIW + PDR001 400 mg
Arm/Group Description	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001
Number of Participants Analyzed [units: participants]	47
Time to reach maximum serum concentration (Tmax) of PDR001 (units: hours)	**Median (Full Range)**

Cycle 1 Day 1 (n=47)	1.15 (1 to 332)
Cycle 3 Day 1 (n=23)	1.08 (0.867 to 1.33)

Area under the serum concentration-time curve from time zero to 28 days post-dose (AUC28d) of PDR001

Description: PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. For PDR001, PK parameters were summarized only for the TIW schedule for the combination arm.

Time Frame: From pre-dose up to 672 hours post dose on Cycle 1 Day 1 and Cycle 3 Day 1. The duration of each cycle was 28 days.

	All NIZ985 1 µg/kg TIW + PDR001 400 mg
Arm/Group Description	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001
Number of Participants Analyzed [units: participants]	47
Area under the serum concentration-time curve from time zero to 28 days post-dose (AUC28d) of PDR001 (units: h*µg/mL)	**Geometric Mean** **(Geometric Coefficient of Variation)**
Cycle 1 Day 1 (n=47)	23600 (25.3%)
Cycle 3 Day 1 (n=23)	45900 (25.8%)

Number of participants with anti-NIZ985 antibodies

Description: Immunogenicity was evaluated in serum in a validated three-tiered assay approach. Samples were screened for potential anti-NIZ985 antibodies and positive screen results were confirmed using a confirmatory assay. For confirmed ADA positive samples, titers were determined. Patient ADA status was defined as follows: • ADA-negative at baseline: ADA-negative sample at baseline • ADA-positive at baseline: ADA-positive sample at baseline • ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline determinant sample, all of which are ADA-negative samples • Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive = ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample

Time Frame From start of treatment until end of treatment, assessed up to 2 years for NIZ985 single agent arm and 2.8 years for combination arm

	NIZ985 0.25 µg/kg TIW	NIZ985 0.5 µg/kg TIW	NIZ985 1 µg/kg TIW	NIZ985 2 µg/kg TIW	NIZ985 4 µg/kg TIW	NIZ985 2 µg/kg Weekly	NIZ985 4 µg/kg Weekly	NIZ985 6 µg/kg Weekly	NIZ985 10 µg/kg Weekly	NIZ985 1 µg/kg TIW + PDR001 400 mg	NIZ985 2 µg/kg Weekly + PDR001 400 mg	NIZ985 4 µg/kg Weekly + PDR001 400 mg	NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant	NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	1	1	5	3	2	2	3	3	3	11	4	5	24	9
Number of participants with anti-	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**	**Count of Participants (Not**

NIZ985 antibodies (units: participants)	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**	**Applicable)**
ADA-negative at baseline	1 (100%)	1 (100%)	5 (100%)	3 (100%)	2 (100%)	2 (100%)	3 (100%)	3 (100%)	3 (100%)	11 (100%)	4 (100%)	5 (100%)	24 (100%)	9 (100%)
ADA-positive at baseline	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
ADA-negative post-baseline	1 (100%)	1 (100%)	4 (80%)	3 (100%)	2 (100%)	2 (100%)	1 (33.33%)	2 (66.67%)	2 (66.67%)	7 (63.64%)	1 (25%)	4 (80%)	20 (83.33%)	6 (66.67%)
Treatment-induced ADA-positive	0 (%)	0 (%)	1 (20%)	0 (%)	0 (%)	0 (%)	2 (66.67%)	1 (33.33%)	1 (33.33%)	4 (36.36%)	3 (75%)	1 (20%)	4 (16.67%)	3 (33.33%)
Treatment-boosted ADA-positive	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Number of participants with anti-PDR001 antibodies

Description

Immunogenicity was evaluated in serum in a validated three-tiered assay approach. Samples were screened for potential anti-PDR001 antibodies and positive screen results were confirmed using a confirmatory assay. For confirmed ADA positive samples, titers were determined. Patient ADA status was defined as follows: • ADA-negative at baseline: ADA-negative sample at baseline • ADA-positive at baseline: ADA-positive sample at baseline • ADA-negative post-baseline: patient with ADA-negative sample at baseline and at least 1 post baseline determinant sample, all of which are ADA-negative samples • Treatment-induced ADA-positive = ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive = ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample

Time Frame From start of treatment until end of treatment, assessed up to 2.8 years

	NIZ985 1 µg/kg TIW + PDR001 400 mg	NIZ985 2 µg/kg Weekly + PDR001 400 mg	NIZ985 4 µg/kg Weekly + PDR001 400 mg	NIZ985 1 µg/kg TIW + PDR001 400 mg - Resistant	NIZ985 1 µg/kg TIW + PDR001 400 mg - Sensitive
Arm/Group Description	Dose escalation part, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors resistant to anti-PD-1 therapy	Dose expansion part, NIZ985 1 µg/kg TIW in combination with PDR001 in tumors sensitive to anti-PD-1 therapy
Number of Participants Analyzed [units: participants]	10	3	5	21	8
Number of participants with anti-PDR001 antibodies (units: participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
ADA-negative at baseline	10 (100%)	3 (100%)	5 (100%)	20 (95.24%)	8 (100%)
ADA-positive at baseline	0 (%)	0 (%)	0 (%)	1 (4.76%)	0 (%)
ADA-negative post-baseline	6 (60%)	3 (100%)	5 (100%)	17 (80.95%)	7 (87.5%)
Treatment-induced ADA-positive	4 (40%)	0 (%)	0 (%)	3 (14.29%)	1 (12.5%)
Treatment-boosted ADA-positive	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)

Safety Results

Time Frame	From first dose of study medication up to 30 days after last dose (NIZ985 single agent arm) and up to 150 days after last dose (combination arm), with a maximum duration of 2.1 years for NIZ985 single agent and 3.2 years for combination arm.
Source Vocabulary for Table Default	MedDRA (25.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	NIZ985 0.25 µg/kg TIW N = 1	**NIZ985 0.5 µg/kg TIW N = 2**	**NIZ985 1 µg/kg TIW N = 6**	**NIZ985 2 µg/kg TIW N = 3**	**NIZ985 4 µg/kg TIW N = 2**	**NIZ985 2 µg/kg Weekly N = 3**	**NIZ985 4 µg/kg Weekly N = 3**	**NIZ985 6 µg/kg Weekly N = 3**	**NIZ985 10 µg/kg Weekly N = 4**	**All NIZ985 1 µg/kg TIW + PDR001 400 mg N = 47**	**NIZ985 2 µg/kg Weekly + PDR001 400 mg N = 4**	**NIZ985 4 µg/kg Weekly + PDR001 400 mg N = 5**
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Total Number Affected	0	0	0	0	1	2	0	2	2	19	2	4
Total Number At Risk	1	2	6	3	2	3	3	3	4	47	4	5

NOVARTIS

Serious Adverse Events

	NIZ985 0.25 µg/kg TIW N = 1	NIZ985 0.5 µg/kg TIW N = 2	NIZ985 1 µg/kg TIW N = 6	NIZ985 2 µg/kg TIW N = 3	NIZ985 4 µg/kg TIW N = 2	NIZ985 2 µg/kg Weekly N = 3	NIZ985 4 µg/kg Weekly N = 3	NIZ985 6 µg/kg Weekly N = 3	NIZ985 10 µg/kg Weekly N = 4	All NIZ985 1 µg/kg TIW + PDR001 400 mg N = 47	NIZ985 2 µg/kg Weekly + PDR001 400 mg N = 4	NIZ985 4 µg/kg Weekly + PDR001 400 mg N = 5
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Total # Affected by any Serious Adverse Event	0	1	1	2	1	1	1	1	4	19	3	1
Total # at Risk by any Serious Adverse Event	1	2	6	3	2	3	3	3	4	47	4	5
Blood and lymphatic system disorders												
Anaemia	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Leukocytosis	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Cardiac disorders												

Atrial fibrillation	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Sinus tachycardia	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Eye disorders												
Vision blurred	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders												
Abdominal pain	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00 %)	3 (6.38 %)	1 (25.00 %)	0 (0.00%)
Ascites	0 (0.00 %)	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 (4.26 %)	0 (0.00%)	0 (0.00%)
Constipation	0 (0.00 %)	0 (0.00%)	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%)
Dysphagia	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Gastrointestinal 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%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Intestinal obstruction	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%)
Nausea	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Oesophageal stenosis	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Small intestinal obstruction	0 (0.00 %)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Upper gastrointestinal haemorrhage	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 %)	1 (25.00 %)	0 (0.00%)
General disorders and												

administration site conditions												
Chest 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%)	2 (4.26 %)	0 (0.00%)	0 (0.00%)
Fatigue	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 (50.00 %)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Multiple organ dysfunction syndrome	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%)
Non-cardiac chest pain	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%)
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 (25.00 %)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Pyrexia	0 (0.00 %)	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 (4.26 %)	0 (0.00%)	1 (20.00 %)
Hepatobiliary disorders												
Hyperbilirubinaemia	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Infections and infestations												
Diverticulitis	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%)
Pneumonia	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Sepsis	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	1 (20.00 %)
Injury, poisoning and procedural complications												
Fall	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)

Wrong product administered	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Investigations												
Alanine aminotransferase increased	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%)
Aspartate aminotransferase increased	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%)
Blood alkaline phosphatase increased	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%)
Blood bilirubin 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 (2.13 %)	0 (0.00%)	0 (0.00%)
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 (2.13 %)	0 (0.00%)	0 (0.00%)
Troponin 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 (2.13 %)	0 (0.00%)	0 (0.00%)
Urine output decreased	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
White blood cell 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%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders												
Dehydration	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Hyperammonaemia	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Hyponatraemia	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)

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%)	0 (0.00%)	0 (0.00%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Flank 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%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Joint effusion	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Nervous system disorders												
Encephalopathy	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Ischaemic stroke	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%)
Seizure	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders												
Acute kidney injury	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders												
Aspiration	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%)
Bronchial obstruction	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Chronic obstructive	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)

pulmonary disease												
Dyspnoea	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Hypoxia	0 (0.00 %)	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 (2.13 %)	0 (0.00%)	0 (0.00%)
Productive cough	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
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%)	1 (25.00 %)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Respiratory 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%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Tracheal stenosis	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders												
Dermatitis bullous	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%)
Purpura	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%)
Vascular disorders												
Embolism	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13 %)	0 (0.00%)	0 (0.00%)
Vasculitis	0 (0.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00 %)	0 (0.00%)	0 (0.00%)

Other (Not Including Serious) Adverse Events

Frequent Event Reporting Threshold 5%

	NIZ985 0.25 µg/kg TIW N = 1	NIZ985 0.5 µg/kg TIW N = 2	NIZ985 1 µg/kg TIW N = 6	NIZ985 2 µg/kg TIW N = 3	NIZ985 4 µg/kg TIW N = 2	NIZ985 2 µg/kg Weekly N = 3	NIZ985 4 µg/kg Weekly N = 3	NIZ985 6 µg/kg Weekly N = 3	NIZ985 10 µg/kg Weekly N = 4	All NIZ985 1 µg/kg TIW + PDR001 400 mg N = 47	NIZ985 2 µg/kg Weekly + PDR001 400 mg N = 4	NIZ985 4 µg/kg Weekly + PDR001 400 mg N = 5
Arm/Group Description	Dose escalation part, NIZ985 0.25 µg/kg TIW	Dose escalation part, NIZ985 0.5 µg/kg TIW	Dose escalation part, NIZ985 1 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg TIW	Dose escalation part, NIZ985 4 µg/kg TIW	Dose escalation part, NIZ985 2 µg/kg weekly	Dose escalation part, NIZ985 4 µg/kg weekly	Dose escalation part, NIZ985 6 µg/kg weekly	Dose escalation part, NIZ985 10 µg/kg weekly	Dose escalation and dose expansion parts, NIZ985 1 µg/kg TIW in combination with PDR001	Dose escalation part, NIZ985 2 µg/kg weekly in combination with PDR001	Dose escalation part, NIZ985 4 µg/kg weekly in combination with PDR001
Total # Affected by any Other Adverse Event	1	2	6	3	2	3	3	3	4	47	4	5
Total # at Risk by any Other Adverse Event	1	2	6	3	2	3	3	3	4	47	4	5
Blood and lymphatic system disorders												
Anaemia	0 (0.00%)	1 (50.00%)	1 (16.67%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	8 (17.02%)	2 (50.00%)	1 (20.00%)
Lymph node pain	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Lymphadenopathy	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%)
Cardiac disorders												

Atrial fibrillation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Sinus tachycardia	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%)	2 (4.26%)	1 (25.00%)	0 (0.00%)
Endocrine disorders												
Hypothyroidism	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Eye disorders												
Dry eye	1 (100.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Eyelid 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%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Vision blurred	1 (100.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	1 (20.00%)
Gastrointestinal disorders												
Abdominal discomfort	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%)
Abdominal distension	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	5 (10.64%)	2 (50.00%)	1 (20.00%)
Abdominal pain	1 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (100.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	14 (29.79%)	1 (25.00%)	1 (20.00%)
Abdominal pain lower	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
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%)	5 (10.64%)	1 (25.00%)	0 (0.00%)
Anal incontinence	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%)
Cheilitis	0 (0.00%)	0 (0.00%)	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%)

Constipation	0 (0.00%)	0 (0.00%)	2 (33.33%)	2 (66.67%)	1 (50.00%)	1 (33.33%)	2 (66.67%)	0 (0.00%)	2 (50.00%)	3 (6.38%)	2 (50.00%)	0 (0.00%)
Diarrhoea	1 (100.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	2 (50.00%)	14 (29.79%)	1 (25.00%)	1 (20.00%)
Dyspepsia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Enterocolitis	0 (0.00%)	0 (0.00%)	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%)
Large intestinal obstruction	0 (0.00%)	0 (0.00%)	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%)
Mouth haemorrhage	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%)
Nausea	0 (0.00%)	1 (50.00%)	2 (33.33%)	1 (33.33%)	1 (50.00%)	2 (66.67%)	3 (100.00%)	1 (33.33%)	1 (25.00%)	19 (40.43%)	2 (50.00%)	2 (40.00%)
Odynophagia	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%)
Oesophageal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oesophageal stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oral dysaesthesia	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%)	0 (0.00%)	0 (0.00%)
Oral 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%)	1 (25.00%)	0 (0.00%)
Proctalgia	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%)
Stomatitis	0 (0.00%)	0 (0.00%)	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%)
Swollen tongue	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)

Tongue coated	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tongue 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%)	0 (0.00%)	0 (0.00%)	1 (20.00%)
Toothache	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	2 (33.33%)	1 (33.33%)	0 (0.00%)	2 (66.67%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	17 (36.17%)	1 (25.00%)	3 (60.00%)
General disorders and administration site conditions												
Asthenia	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Chills	0 (0.00%)	1 (50.00%)	4 (66.67%)	3 (100.00%)	2 (100.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	3 (75.00%)	11 (23.40%)	1 (25.00%)	3 (60.00%)
Fatigue	0 (0.00%)	1 (50.00%)	4 (66.67%)	3 (100.00%)	1 (50.00%)	2 (66.67%)	2 (66.67%)	2 (66.67%)	3 (75.00%)	25 (53.19%)	3 (75.00%)	2 (40.00%)
Influenza like illness	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	1 (25.00%)	15 (31.91%)	1 (25.00%)	2 (40.00%)
Injection site erythema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	6 (12.77%)	0 (0.00%)	0 (0.00%)
Injection site pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injection site pruritus	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%)	4 (8.51%)	0 (0.00%)	0 (0.00%)
Injection site reaction	1 (100.00%)	2 (100.00%)	6 (100.00%)	3 (100.00%)	2 (100.00%)	1 (33.33%)	3 (100.00%)	3 (100.00%)	2 (50.00%)	41 (87.23%)	4 (100.00%)	5 (100.00%)
Injection site warmth	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%)
Localised 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 (25.00%)	3 (6.38%)	0 (0.00%)	0 (0.00%)

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%)	2 (4.26%)	1 (25.00%)	1 (20.00%)
Nodule	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%)
Non-cardiac chest pain	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (50.00%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	3 (75.00%)	5 (10.64%)	0 (0.00%)	2 (40.00%)
Pain	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Pyrexia	0 (0.00%)	1 (50.00%)	4 (66.67%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	0 (0.00%)	2 (50.00%)	8 (17.02%)	3 (75.00%)	1 (20.00%)
Swelling face	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Hepatobiliary disorders												
Biliary obstruction	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%)
Hepatic 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%)	1 (20.00%)
Hyperbilirubinaemia	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%)
Infections and infestations												
Candida 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%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
Cellulitis	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Folliculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Fungal skin 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%)	1 (20.00%)

Gingivitis	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%)
Perichondritis	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%)
Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
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%)	1 (20.00%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	5 (10.64%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications												
Animal bite	1 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fall	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	2 (50.00%)	2 (4.26%)	0 (0.00%)	2 (40.00%)
Procedural 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%)	2 (4.26%)	1 (25.00%)	0 (0.00%)
Skin abrasion	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Skin laceration	0 (0.00%)	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 (2.13%)	1 (25.00%)	0 (0.00%)
Sunburn	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Investigations												
Aspartate aminotransferase 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%)	3 (6.38%)	0 (0.00%)	1 (20.00%)

Biopsy chest wall	0 (0.00%)	0 (0.00%)	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%)
Biopsy skin	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Blood alkaline phosphatase 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%)	1 (25.00%)	4 (8.51%)	0 (0.00%)	0 (0.00%)
Blood bilirubin increased	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Blood creatinine increased	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%)	4 (8.51%)	0 (0.00%)	0 (0.00%)
Blood lactate dehydrogenase increased	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%)	1 (20.00%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Heart rate increased	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%)
International normalised ratio increased	0 (0.00%)	0 (0.00%)	1 (16.67%)	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%)
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%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	2 (100.00%)	0 (0.00%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	4 (8.51%)	0 (0.00%)	1 (20.00%)
Platelet 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%)	1 (20.00%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	1 (25.00%)	8 (17.02%)	0 (0.00%)	0 (0.00%)

White blood cell 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%)	1 (2.13%)	0 (0.00%)	1 (20.00%)
Metabolism and nutrition disorders												
Acidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Decreased appetite	0 (0.00%)	0 (0.00%)	2 (33.33%)	1 (33.33%)	1 (50.00%)	2 (66.67%)	2 (66.67%)	2 (66.67%)	2 (50.00%)	15 (31.91%)	3 (75.00%)	1 (20.00%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	2 (66.67%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	10 (21.28%)	1 (25.00%)	0 (0.00%)
Hyperglycaemia	1 (100.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.26%)	0 (0.00%)	1 (20.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Hypoalbuminaemia	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%)	2 (4.26%)	1 (25.00%)	1 (20.00%)
Hypocalcaemia	0 (0.00%)	1 (50.00%)	0 (0.00%)	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%)
Hypokalaemia	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	1 (25.00%)	2 (4.26%)	0 (0.00%)	2 (40.00%)
Hypomagnesaemia	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	6 (12.77%)	1 (25.00%)	1 (20.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	3 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (8.51%)	1 (25.00%)	1 (20.00%)
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%)	0 (0.00%)	5 (10.64%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders												

Arthralgia	0 (0.00%)	2 (100.00%)	2 (33.33%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	1 (33.33%)	1 (33.33%)	1 (25.00%)	13 (27.66%)	1 (25.00%)	3 (60.00%)
Back pain	1 (100.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	2 (66.67%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	9 (19.15%)	0 (0.00%)	1 (20.00%)
Flank pain	1 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	1 (25.00%)	0 (0.00%)
Groin 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%)	2 (4.26%)	1 (25.00%)	0 (0.00%)
Muscle atrophy	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%)
Muscle spasms	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%)	3 (6.38%)	1 (25.00%)	0 (0.00%)
Muscular weakness	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%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
Musculoskeletal chest 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%)	1 (2.13%)	0 (0.00%)	1 (20.00%)
Myalgia	0 (0.00%)	1 (50.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	12 (25.53%)	1 (25.00%)	1 (20.00%)
Neck pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	4 (8.51%)	0 (0.00%)	1 (20.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	6 (12.77%)	1 (25.00%)	0 (0.00%)
Pain in jaw	0 (0.00%)	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 (2.13%)	0 (0.00%)	1 (20.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)												
Lipoma	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%)

Squamous cell carcinoma	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%)
Tumour pain	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Nervous system disorders												
Cognitive disorder	0 (0.00%)	1 (50.00%)	1 (16.67%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	3 (100.00%)	0 (0.00%)	1 (33.33%)	2 (50.00%)	12 (25.53%)	1 (25.00%)	3 (60.00%)
Dysgeusia	0 (0.00%)	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 (6.38%)	0 (0.00%)	1 (20.00%)
Headache	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	12 (25.53%)	1 (25.00%)	0 (0.00%)
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%)	1 (25.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)
Lethargy	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%)
Paraesthesia	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Peripheral motor neuropathy	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%)
Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)	1 (25.00%)	0 (0.00%)
Tremor	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 (2.13%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders												

Agitation	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%)	1 (25.00%)	0 (0.00%)
Anxiety	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%)	4 (8.51%)	0 (0.00%)	0 (0.00%)
Confusional state	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Delirium	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Insomnia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (8.51%)	0 (0.00%)	0 (0.00%)
Personality change	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%)
Renal and urinary disorders												
Acute kidney injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysuria	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%)
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	1 (20.00%)
Haemoglobinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nephrolithiasis	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Proteinuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders												

Atelectasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchial obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	1 (25.00%)	4 (8.51%)	1 (25.00%)	0 (0.00%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (33.33%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	7 (14.89%)	1 (25.00%)	0 (0.00%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Hypercapnia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	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%)
Nasal congestion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.38%)	0 (0.00%)	1 (20.00%)
Oropharyngeal 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%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
Pleural effusion	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Productive cough	0 (0.00%)	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 (6.38%)	0 (0.00%)	1 (20.00%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis allergic	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%)
Stridor	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tracheal stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Upper-airway cough 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 (2.13%)	0 (0.00%)	1 (20.00%)
Wheezing	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders												
Dry skin	0 (0.00%)	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 (10.64%)	0 (0.00%)	0 (0.00%)
Hyperhidrosis	0 (0.00%)	0 (0.00%)	2 (33.33%)	2 (66.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.38%)	0 (0.00%)	1 (20.00%)
Night sweats	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	4 (8.51%)	1 (25.00%)	0 (0.00%)
Onychomadesis	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%)
Pruritus	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (33.33%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	5 (10.64%)	1 (25.00%)	1 (20.00%)
Purpura	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash	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 (50.00%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	7 (14.89%)	0 (0.00%)	0 (0.00%)
Skin lesion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Skin mass	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%)	1 (2.13%)	0 (0.00%)	0 (0.00%)
Vasculitic rash	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders												

Deep vein thrombosis	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%)	3 (6.38%)	0 (0.00%)	0 (0.00%)
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%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Flushing	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (8.51%)	0 (0.00%)	0 (0.00%)
Hot flush	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (6.38%)	0 (0.00%)	1 (20.00%)
Hypertension	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%)	2 (4.26%)	0 (0.00%)	0 (0.00%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (66.67%)	1 (50.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)	3 (6.38%)	0 (0.00%)	0 (0.00%)

Conclusion:

- Doses up to 10 µg/kg weekly of NIZ985 as single agent and up to 4 µg/kg weekly of NIZ985 in combination with PDR001 400 mg were explored and the safety profile was generally manageable. The RDE of NIZ985 as a single agent and in combination with PDR001 400 mg was determined as 1 µg/kg TIW.
- Evidence of preliminary anti-tumor activity was observed for the combination of NIZ985 and PDR001.
- Exposure of NIZ985 after the first dose increased in an approximately dose-proportional manner over the dose range of 1-4 µg/kg with TIW schedule, and over the dose range of 2-10 µg/kg with weekly schedule, although the data showed large variability. Exposure of NIZ985 did not appear to be affected by co-administration of PDR001.

Date of Clinical Trial Report

2-Jan-2023