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## Sponsor

Novartis Pharmaceuticals

## Generic Drug Name

KAZ954, spartalizumab (PDR001), taminadenant (NIR178) and NZV930

## Trial Indication(s)

Microsatellite stable colorectal cancer (MSS CRC), cholangiocarcinoma, pancreatic cancer, esophageal, esophageal gastric junction (EGJ) or gastric cancer

## Protocol Number

CKAZ954A12101

## Protocol Title

A phase I/Ib, open-label, multi-center, study of KAZ954 as a single agent and in combination with Spartalizumab, NZV930 and NIR178 in patients with advanced solid tumors

## Clinical Trial Phase

Phase 1

## Phase of Drug Development

KAZ985 (phase 1), spartalizumab (phase 3), NIR178 (phase 2) and NZV930 (phase 1)

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## Study Start/End Dates

Study Start Date: February 20, 2020 (Actual)
Primary Completion Date: September 15, 2023 (Actual)
Study Completion Date: September 15, 2023 (Actual)

## Reason for Termination (If applicable)

The study enrollment was halted on 14-Jun-2023, after the enrollment of 77 patients in the dose escalation portion of the study. Study enrollment was halted prior to enrollment into the KAZ954 + NZV930 combination treatment and prior to the expansion part of the study. No patients were receiving treatment at the time of enrollment halt and patient follow-up was to continue as per protocol. Based on the totality of the available data, it was decided not to progress further in the expansion phase of the study. Importantly, the recruitment halt was not a consequence of any safety concern.

## Study Design/Methodology

This was an first in human (FIH), open-label, phase I/Ib, multi-center study of KAZ954 as a single agent and in combination with spartalizumab, NZV930 or NIR178 in patients with MSS CRC, cholangiocarcinoma, pancreatic cancer, esophageal, EGJ or gastric cancer.

In the first part of the study, dose escalation, patients were to be treated with escalating doses of KAZ954 alone and in combination with spartalizumab, NZV930 or NIR178 in order to identify the maximum tolerated dose/recommended dose for expansion (MTD/RD). The dose escalation arm KAZ954+NZV930 was not opened.

In the dose expansion part, patients were to be treated at the RD of KAZ954 as a single agent and in combination with spartalizumab, NZV930 or NIR178. The dose expansion part of the study was not started.

## Centers

13 centers in 8 countries: Singapore(1), United States(5), Japan(1), Italy(2), Spain(1), Taiwan(1), Hong Kong(1), Canada(1)

## Objectives:

The primary objective of the trial was to characterize the safety, tolerability, and maximum tolerated dose/recommended dose for expansion of single agent KAZ954 and KAZ954 in combination with spartalizumab, NIR178 or NZV930.

The secondary objectives were:

- To evaluate the preliminary anti-tumor activity of single agent KAZ954 and KAZ954 in combination with spartalizumab, NIR178 or NZV930
- To determine the pharmacokinetics (PK) and immunogenicity of KAZ954 as a single agent and KAZ954 in combination with spartalizumab, NIR178 or NZV930
- Assess the relationship between PD-L1 expression level in tumor and response to single agent KAZ954 and KAZ954 in combination with spartalizumab, NIR178 or NZV930

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

For this study, the terms “investigational drug” or “study drug” refer to KAZ954, spartalizumab (PDR001), NZV930, and taminadenant (NIR178). The study treatment was defined as KAZ954 alone or in combination with spartalizumab (PDR001), or NIR178.

KAZ954 and spartalizumab were administered by intravenous (IV) infusion over 2 hours and 30 minutes, respectively. NIR178 was taken orally as capsules.

Prior to Cycle 1 Day 1 (C1D1), patients were assigned to one of the following three treatment arms and one of the three KAZ954 schedules:

- Arm A – Single agent KAZ954
- Arm B – Combination KAZ954 + spartalizumab administered once every 4 weeks (Q4W)
- Arm C – Combination KAZ954 + NIR178 administered twice daily (b.i.d.) continuously

- Schedule 1 – KAZ954 every 2 weeks (Q2W)
- Schedule 2 (from release of Protocol Amendment 3) – KAZ954 with single priming dose at C1D1 followed by the experimental dose at Cycle 1 Day 15 (C1D15) and beyond on a Q2W schedule.
- Schedule 3 (from release of Protocol Amendment 3)– KAZ954 with two priming doses – C1D1 and Cycle 1 Day 8 (C1D8) followed by the experimental dose at C1D15 and beyond on a Q2W schedule.

In Schedule 2 and 3, the priming doses were lower than the experimental dose. The use of a priming dose was hypothesized to mitigate the risk of first dose effect.

No patients received treatment with KAZ954 + NZV930 combination because study enrollment was halted prior to enrollment into this arm.

## Statistical Methods

**Safety**: AEs were coded using MedDRA version 26.1 and assessed according to CTCAE version 5.0. AEs were assessed in the Safety Set comprising all patients who received at least one dose of study treatment (i.e. at least one dose of any component of the combination therapy). Patients were analyzed according to the study treatment received.

Tolerability of study drug was assessed by summarizing dose interruptions and dose reductions. Dose intensity of study treatment was also tabulated by treatment group for each component of the study treatment.

Identification of the maximum tolerated dose (MTD) of the study treatment was based upon the estimation of the probability of dose-limiting toxicities (DLTs) for patients in the Dose-determining (DDS) set and took into consideration other safety, clinical, PK and pharmacodynamics (PD) data. The dose escalation part of the study was guided by a Bayesian analysis of DLT data in the DLT period for each study treatment. The DDS for the experimental dose escalation included all patients who received at least one dose of study treatment and met the minimum exposure criterion and had sufficient safety evaluations (as determined by Novartis and Investigator) or experienced a DLT during the DLT-evaluation period.

**Efficacy**: Full analysis set (FAS) was used for the secondary efficacy. The FAS comprised all patients who received at least one dose of study treatment (i.e. at least one dose of any component of the combination therapy). Efficacy was assessed

by the investigator per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) and immune-related Response Evaluation Criteria for Solid Tumors (iRECIST).

**Pharmacokinetics**: All PK data analysis and PK summary statistics were based on the Pharmacokinetic analysis set (PAS). The PAS included all patients who provided an evaluable PK profile. A profile was considered evaluable if all of the following conditions were satisfied:

• Patient received one of the planned treatments
• Patient provided at least one primary PK parameter

**Immunogenicity**: The immunogenicity was summarized by treatment group for each study treatment.

**PD-L1 expression and anti-tumor activity endpoints (ORR and PFS)**: Programmed Death-Ligand 1 (PD-L1) expression at baseline was summarized by mean of descriptive statistics for responders and non-responders based on overall response rate (ORR/iORR). In addition, progression free survival (PFS) was summarized for patients with high/medium/low PD-L1 expression at baseline using the Kaplan Meier method.

## Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

- Patients with metastatic and/or advanced malignancies not amenable to curative treatment by surgery.
- Must have a site of disease amenable to biopsy and be a candidate for tumor biopsy according to the treating institution's guidelines. Patient must be willing to undergo a new tumor biopsy at screening and during the study.
- ECOG Performance Status of <2.

Exclusion Criteria:

- Presence of symptomatic central nervous system (CNS) metastases, or CNS metastases that require concurrent treatment - including surgery, radiation and/or corticosteroids.

- History of severe hypersensitivity reaction to any ingredient of study drug(s) and other mAbs and/or their excipients. Impaired cardiac function
- HIV
- Known history of tuberculosis
- Systemic chronic steroid therapy

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# Participant Flow Table

## Overall Study

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. | |
| **Started** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 |
| **Completed** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Not Completed** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 |
| Adverse Event | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 5 |
| Death | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 4 |
| New therapy for study indication | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| Patient went to hospice | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 2 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Progressive disease | 3 | 3 | 4 | 9 | 5 | 5 | 7 | 3 | 3 | 7 | 2 | 6 | 6 | 63 |
| Withdrawal by Subject | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 |
| Withdrew from trial | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |

## Baseline Characteristics

| | **KAZ954 30 mg** | **KAZ954 50 mg** | **KAZ954 100 mg** | **KAZ954 150 mg** | **KAZ954 300 mg** | **KAZ954 600 mg** | **KAZ954 1200 mg** | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg + PDR001 400 mg** | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** | **Total** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. | |
| **Number of Participants [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 |
| Baseline Analysis | | | | | | | | | | | | | | |

| Population Description | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Age Continuous**<br>(units: years)<br>Analysis Population Type: Participants<br>Mean ± Standard Deviation | 57.7± 4.73 | 58.3± 6.18 | 60.0±1 2.41 | 61.2±1 0.47 | 56.6±1 3.50 | 60.2±1 2.73 | 53.7± 9.57 | 61.0±9.3 0 | 53.3±11. 41 | 54.8±15. 10 | 65.3±8. 77 | 58.0±1 0.92 | 57.8±1 3.04 | 59.3±1 0.95 |
| **Age, Customized**<br>(units: participants)<br>Analysis Population Type: Participants<br>Count of Participants (Not Applicable) | | | | | | | | | | | | | | |
| 18 - 64 years | 3 | 3 | 3 | 6 | 3 | 3 | 5 | 3 | 3 | 7 | 2 | 4 | 4 | 49 |
| 65 - 84 years | 0 | 1 | 1 | 5 | 2 | 3 | 5 | 2 | 1 | 2 | 2 | 2 | 2 | 28 |
| >84 years | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Sex: Female, Male**<br>(units: participants)<br>Analysis Population Type: Participants<br>Count of Participants (Not Applicable) | | | | | | | | | | | | | | |
| Female | 0 | 2 | 2 | 5 | 2 | 3 | 8 | 2 | 1 | 4 | 2 | 4 | 2 | 37 |
| Male | 3 | 2 | 2 | 6 | 3 | 3 | 2 | 3 | 3 | 5 | 2 | 2 | 4 | 40 |
| **Race/Ethnicity, Customized**<br>(units: participants)<br>Analysis Population Type: Participants<br>Count of Participants (Not Applicable) | | | | | | | | | | | | | | |
| Asian | 1 | 2 | 2 | 2 | 1 | 2 | 1 | 1 | 2 | 0 | 1 | 1 | 1 | 17 |
| Black Or African American | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| White | 2 | 2 | 1 | 8 | 4 | 4 | 9 | 4 | 2 | 9 | 3 | 5 | 5 | 58 |
| Unknown | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |

| Study Specific Characteristic<br>Diagnosis of disease<br>(units: participants)<br>Analysis Population Type: Participants<br>Count of Participants (Not Applicable) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cholangiocarcinoma | 0 | 1 | 0 | 3 | 0 | 0 | 3 | 0 | 1 | 0 | 1 | 1 | 0 | 10 |
| Colorectal cancer | 2 | 2 | 2 | 5 | 1 | 4 | 2 | 2 | 2 | 2 | 2 | 5 | 5 | 36 |
| Esophageal cancer | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 |
| Pancreatic cancer | 0 | 0 | 2 | 3 | 4 | 1 | 5 | 3 | 1 | 7 | 1 | 0 | 1 | 28 |

# Primary Outcome Result(s)

## Number of participants with Dose-Limiting Toxicities (DLTs)

| | |
|---|---|
| Description | A dose-limiting toxicity (DLT) is defined as an adverse event or abnormal laboratory value of Common Terminology Criteria for Adverse Events (CTCAE) grade ≥ 3 assessed as unrelated to disease, disease progression, inter-current illness or concomitant medications, which occurs within the DLT period. The DLT period for Schedule 1 is 28 days and covers two infusions. The DLT period for Schedule 2 and Schedule 3 is 35 days to cover two infusions of the Experimental dose. Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher. |
| Time Frame | Up to 35 days |
| Analysis Population Description | All patients who received at least one dose of study treatment, and who met the minimum exposure criterion defined in the protocol and had sufficient safety evaluations or had experienced a DLT during the DLT evaluation period. |

| KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + | KAZ954 600 mg + | KAZ954 1200 mg + | KAZ954 300 mg + | KAZ954 600 mg + | KAZ954 600 mg + |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | PDR001 400 mg | PDR001 400 mg | PDR001 400 mg | NIR178 160 mg | NIR178 160 mg | NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 3 | 10 | 5 | 6 | 7 | 4 | 3 | 7 | 2 | 5 | 5 |
| **Number of participants with Dose-Limiting Toxicities (DLTs)** (units: participants) | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** |
| Any DLT | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (16.67%) | 0 (%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| - Disseminated | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (16.67%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| intravascular coagulation | | | | | | | | | | | | | |
| - Myocarditis | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |

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

| | |
|---|---|
| Description | Number of participants with AEs (any AE regardless of seriousness) and SAEs, including changes from baseline in vital signs, electrocardiograms and laboratory results qualifying and reported as AEs. The on-treatment period is defined from the day of first administration of study treatment up to 30 days after the date of its last administration. |
| Time Frame | Up to approximately 52 weeks (KAZ954 single agent), 20 weeks (KAZ954+PDR001) and 24 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | **KAZ954 30 mg** | **KAZ954 50 mg** | **KAZ954 100 mg** | **KAZ954 150 mg** | **KAZ954 300 mg** | **KAZ954 600 mg** | **KAZ954 1200 mg** | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg + PDR001 400 mg** | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |

| **Participants Analyzed [units: participants]** | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number of participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) during the on-treatment period** (units: participants) | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** |
| AEs | 3 (100%) | 4 (100%) | 4 (100%) | 11 (100%) | 5 (100%) | 6 (100%) | 10 (100%) | 5 (100%) | 4 (100%) | 9 (100%) | 4 (100%) | 6 (100%) | 6 (100%) |
| Treatment-related AEs | 3 (100%) | 4 (100%) | 4 (100%) | 8 (72.73%) | 5 (100%) | 5 (83.33%) | 8 (80%) | 5 (100%) | 3 (75%) | 5 (55.56%) | 3 (75%) | 4 (66.67%) | 6 (100%) |
| SAEs | 1 (33.33%) | 1 (25%) | 4 (100%) | 6 (54.55%) | 3 (60%) | 3 (50%) | 5 (50%) | 4 (80%) | 2 (50%) | 4 (44.44%) | 3 (75%) | 4 (66.67%) | 3 (50%) |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Treatment-related SAEs | 1 (33.33%) | 0 (%) | 3 (75%) | 2 (18.18%) | 1 (20%) | 3 (50%) | 1 (10%) | 3 (60%) | 1 (25%) | 2 (22.22%) | 0 (%) | 1 (16.67%) | 3 (50%) |
| Fatal SAEs | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (20%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| Treatment-related fatal SAEs | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |

## Number of participants with dose reductions and dose interruptions of KAZ954

| | |
|---|---|
| Description | Number of participants with at least one dose reduction and at least one dose interruption of KAZ954. Dose or schedule adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of KAZ954 |

| | **KAZ954 30 mg** | **KAZ954 50 mg** | **KAZ954 100 mg** | **KAZ954 150 mg** | **KAZ954 300 mg** | **KAZ954 600 mg** | **KAZ954 1200 mg** | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg + PDR001 400 mg** | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab | KAZ954 600 mg IV Q2W in combination with spartalizumab | KAZ954 1200 mg IV Q2W in combination with spartalizumab | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg |

| | | | | | | | | 400 mg IV Q4W | 400 mg IV Q4W | 400 mg IV Q4W | oral b.i.d. | oral b.i.d. | oral b.i.d. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Number of participants with dose reductions and dose interruptions of KAZ954** (units: participants) | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** |
| At least one dose reduction or interruption | 0 (%) | 0 (%) | 2 (50%) | 1 (9.09%) | 1 (20%) | 1 (16.67%) | 2 (20%) | 1 (20%) | 2 (50%) | 2 (22.22%) | 1 (25%) | 0 (%) | 0 (%) |
| At least one dose reduction | 0 (%) | 0 (%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 1 (10%) | 0 (%) | 1 (25%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| At least one | 0 (%) | 0 (%) | 1 (25%) | 1 (9.09%) | 1 (20%) | 1 (16.67%) | 2 (20%) | 1 (20%) | 1 (25%) | 2 (22.22%) | 1 (25%) | 0 (%) | 0 (%) |

dose
interrupti
on

## Number of participants with dose reductions and dose interruptions of PDR001

| | |
|---|---|
| Description | Number of participants with at least one dose reduction and at least one dose interruption of PDR001. Dose or schedule adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule. Dose reductions were not permitted for PDR001. |
| Time Frame | Up to approximately 16 weeks |
| Analysis Population Description | All patients who received at least one dose of PDR001 |

| | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg + PDR001 400 mg** |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W |
| **Number of Participants Analyzed [units: participants]** | 5 | 4 | 9 |
| **Number of participants with dose reductions and dose interruptions of PDR001** (units: participants) | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** |
| At least one dose reduction or interruption | 0 (%) | 1 (25%) | 0 (%) |
| At least one dose reduction | 0 (%) | 1 (25%) | 0 (%) |
| At least one dose interruption | 0 (%) | 1 (25%) | 0 (%) |

## Number of participants with dose reductions and dose interruptions of NIR178

| | |
|---|---|
| Description | Number of participants with at least one dose reduction and at least one dose interruption of NIR178. Dose or schedule adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule. |
| Time Frame | Up to approximately 18 weeks |
| Analysis Population Description | All patients who received at least one dose of NIR178 |

| | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 4 | 6 | 6 |
| **Number of participants with dose reductions and dose interruptions of NIR178** (units: participants) | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** | **Count of Participants (Percentage)** |
| At least one dose reduction or interruption | 1 (25%) | 1 (16.67%) | 2 (33.33%) |
| At least one dose reduction | 1 (25%) | 1 (16.67%) | 1 (16.67%) |
| At least one dose interruption | 1 (25%) | 1 (16.67%) | 2 (33.33%) |

## Dose intensity of KAZ954

| | |
|---|---|
| Description | Dose intensity of KAZ954 was calculated as cumulative actual dose in milligrams divided by duration of exposure in days. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of KAZ954 |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Dose intensity of KAZ954** (units: mg/day) | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** |
| | 2.14 (2.1 to 2.14) | 3.57 (3.0 to 3.6) | 6.35 (3.4 to 7.1) | 10.71 (8.6 to 15.1) | 17.86 (15.9 to 20.0) | 32.14 (7.1 to 38.4) | 58.25 (7.1 to 74.5) | 17.54 (14.3 to 17.9) | 27.40 (4.6 to 33.3) | 61.62 (7.1 to 67.3) | 16.07 (12.5 to 18.6) | 33.64 (7.1 to 39.3) | 33.93 (7.1 to 35.7) |

## Dose intensity of PDR001

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

Time Frame: Up to approximately 16 weeks

| | |
|---|---|
| Analysis Population Description | All patients who received at least one dose of PDR001 |

| | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W |
| **Number of Participants Analyzed [units: participants]** | 5 | 4 | 9 |
| **Dose intensity of PDR001** (units: mg/day) | **Median (Full Range)** | **Median (Full Range)** | **Median (Full Range)** |
| | 14.29 (12.7 to 14.3) | 14.04 (13.1 to 14.3) | 14.29 (14.0 to 16.2) |

## Dose intensity of NIR178

| | |
|---|---|
| Description | Dose intensity of NIR178 was calculated as cumulative actual dose in milligrams divided by duration of exposure in days. |
| Time Frame | Up to approximately 18 weeks |
| Analysis Population Description | All patients who received at least one dose of NIR178 |

| | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 4 | 6 | 6 |

| Dose intensity of NIR178 (units: mg/day) | Median (Full Range) | Median (Full Range) | Median (Full Range) |
|---|---|---|---|
| | 311.11 (225.2 to 320.0) | 320.00 (301.3 to 320.0) | 480.00 (428.6 to 480.0) |

# Secondary Outcome Result(s)

## Overall Response Rate (ORR) per RECIST v1.1

| | |
|---|---|
| Description | ORR is the percentage of patients with a best overall response of complete response (CR) or partial response (PR), based on local investigator assessment per Response Evaluation Criteria for 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 diameter of all target lesions, taking as reference the baseline sum of diameters. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Overall Response Rate (ORR) per RECIST v1.1** (units: percentage of participants) | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** |
| | 0 (0.0 to 63.2) | 0 (0.0 to 52.7) | 0 (0.0 to 52.7) | 0 (0.0 to 23.8) | 0 (0.0 to 45.1) | 0 (0.0 to 39.3) | 0 (0.0 to 25.9) | 0 (0.0 to 45.1) | 0 (0.0 to 52.7) | 0 (0.0 to 28.3) | 0 (0.0 to 52.7) | 0 (0.0 to 39.3) | 0 (0.0 to 39.3) |

## Overall Response Rate (ORR) per iRECIST

| | |
|---|---|
| Description | ORR is the percentage of patients with a best overall response of complete response (iCR) or partial response (iPR), based on local investigator assessment per immune-related RECIST (iRECIST). For iRECIST, the principles used to determine objective tumor response are largely unchanged from RECIST v1.1, while the major change of iRECIST is the concept of 'resetting the bar' if RECIST v1.1 progression is followed by tumor shrinkage. Unlike RECIST v1.1, iRECIST requires the confirmation of progression. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Overall Response Rate (ORR) per iRECIST** (units: percentage of participants) | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** |
| | 0 (0.0 to 63.2) | 0 (0.0 to 52.7) | 0 (0.0 to 52.7) | 0 (0.0 to 23.8) | 0 (0.0 to 45.1) | 0 (0.0 to 39.3) | 0 (0.0 to 25.9) | 0 (0.0 to 45.1) | 0 (0.0 to 52.7) | 0 (0.0 to 28.3) | 0 (0.0 to 52.7) | 0 (0.0 to 39.3) | 0 (0.0 to 39.3) |

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## Disease Control Rate (DCR) per RECIST v1.1

| | |
|---|---|
| Description | DCR is the percentage of patients with a best overall response of complete response (CR), partial response (PR) or stable disease (SD), based on local investigator assessment per Response Evaluation Criteria for 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 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 | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | **KAZ954 30 mg** | **KAZ954 50 mg** | **KAZ954 100 mg** | **KAZ954 150 mg** | **KAZ954 300 mg** | **KAZ954 600 mg** | **KAZ954 1200 mg** | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg + PDR001 400 mg** | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Disease Control** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** | **Number (90%** |

| Rate (DCR) per RECIST v1.1 (units: percentage of participants) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) | Confidence Interval) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 (0.0 to 63.2) | 0 (0.0 to 52.7) | 25.0 (1.3 to 75.1) | 36.4 (13.5 to 65.0) | 40.0 (7.6 to 81.1) | 16.7 (0.9 to 58.2) | 10.0 (0.5 to 39.4) | 20.0 (1.0 to 65.7) | 0 (0.0 to 52.7) | 11.1 (0.6 to 42.9) | 0 (0.0 to 52.7) | 16.7 (0.9 to 58.2) | 0 (0.0 to 39.3) |

## Disease Control Rate (DCR) per iRECIST

| | |
|---|---|
| Description | DCR is the percentage of patients with a best overall response of complete response (iCR), partial response (iPR), stable disease (iSD), based on local investigator assessment per immune-related RECIST (iRECIST). For iRECIST, the principles used to determine objective tumor response are largely unchanged from RECIST v1.1, while the major change of iRECIST is the concept of 'resetting the bar' if RECIST v1.1 progression is followed by tumor shrinkage. Unlike RECIST v1.1, iRECIST requires the confirmation of progression. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizu | KAZ954 600 mg IV Q2W in combination with spartalizu | KAZ954 1200 mg IV Q2W in combination with spartalizu | KAZ954 300 mg IV Q2W in combination with NIR178 | KAZ954 600 mg IV Q2W in combination with NIR178 | KAZ954 600 mg IV Q2W in combination with NIR178 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | mab 400 mg IV Q4W | mab 400 mg IV Q4W | mab 400 mg IV Q4W | 160 mg oral b.i.d. | 160 mg oral b.i.d. | 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Disease Control Rate (DCR) per iRECIST** (units: percentage of participants) | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** |
| | 0 (0.0 to 63.2) | 0 (0.0 to 52.7) | 25.0 (1.3 to 75.1) | 36.4 (13.5 to 65.0) | 40.0 (7.6 to 81.1) | 16.7 (0.9 to 58.2) | 10.0 (0.5 to 39.4) | 20.0 (1.0 to 65.7) | 0 (0.0 to 52.7) | 11.1 (0.6 to 42.9) | 0 (0.0 to 52.7) | 16.7 (0.9 to 58.2) | 0 (0.0 to 39.3) |

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

| | |
|---|---|
| Description | For assessment per RECIST v1.1, PFS is the time from date of start of treatment to the date of event defined as the first progression or death due to any cause. If a subject had not had an event, PFS was censored at the date of last adequate tumor assessment. PFS was analyzed using the Kaplan-Meier method. |
| Time Frame | Up to approximately 52 weeks (KAZ954 single agent), 20 weeks (KAZ954+PDR001) and 24 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Progression-Free Survival (PFS) per RECIST v1.1** (units: months) | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** |
| | 1.6 (1.6 to NA)[1] | 1.4 (1.0 to NA)[1] | 1.7 (1.0 to NA)[1] | 1.8 (1.0 to 6.9) | 1.6 (1.2 to NA)[1] | 1.8 (1.5 to NA)[1] | 1.8 (0.5 to 2.4) | 2.1 (1.6 to NA)[1] | 1.8 (1.6 to NA)[1] | 1.7 (0.2 to 1.9) | 2.0 (1.6 to NA)[1] | 1.7 (1.4 to NA)[1] | 1.6 (0.5 to NA)[1] |

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

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## Progression-Free Survival (iPFS) per iRECIST

| | |
|---|---|
| Description | For assessment per iRECIST, iPFS is the time from date of start of treatment to the date of event defined as the first documented confirmed progression or death due to any cause. If a subject had not had an event, iPFS was censored at the date of last adequate tumor assessment. PFS was analyzed using the Kaplan-Meier method. |
| Time Frame | Up to approximately 52 weeks (KAZ954 single agent), 20 weeks (KAZ954+PDR001) and 24 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **Progression-Free Survival** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confiden** | **Median (90% Confiden** | **Median (90% Confiden** | **Median (90% Confidence** | **Median (90% Confidence** | **Median (90% Confidence** |

| (iPFS) per iRECIST (units: months) | Interval ) | Interval ) | Interval ) | Interval ) | Interval ) | Interval ) | Interval ) | ce Interval) | ce Interval) | ce Interval) | Interval ) | Interval ) | Interval ) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NA (1.6 to NA)[1] | 1.5 (1.2 to NA)[1] | 1.7 (1.0 to NA)[1] | 2.7 (0.6 to 5.6) | 1.6 (1.2 to NA)[1] | 1.8 (1.5 to NA)[1] | 1.8 (0.7 to 2.6) | 2.1 (1.6 to NA)[1] | 1.8 (1.6 to NA)[1] | 1.7 (0.8 to NA)[1] | 2.0 (1.6 to NA)[1] | 1.7 (1.4 to NA)[1] | 1.6 (0.5 to NA)[1] |

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

## Maximum observed serum concentration (Cmax) of KAZ954

| | |
|---|---|
| Description | Pharmacokinetic (PK) parameters were calculated based on free KAZ954 serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 3 Day 1 (C3D1): pre-dose, 1, 24, 72, 168, 240 and 360 hours after the end of the infusion. The duration of the infusion was 2 hours. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received KAZ954 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | KAZ954 4 30 mg | KAZ954 4 50 mg | KAZ954 4 100 mg | KAZ954 4 150 mg | KAZ954 4 300 mg | KAZ954 4 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 4 300 mg + NIR178 160 mg | KAZ954 4 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 4 30 mg IV Q2W | KAZ954 4 50 mg IV Q2W | KAZ954 4 100 mg IV Q2W | KAZ954 4 150 mg IV Q2W | KAZ954 4 300 mg IV Q2W | KAZ954 4 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 4 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 4 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 3 | 10 | 5 | 4 | 8 | 2 | 3 | 7 | 4 | 4 | 4 |
| **Maximum observed serum concentration (Cmax) of KAZ954** (units: µg/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **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=3,4,3,10,5,4,8,2,3,7,4,4,4) | 7.08 (28.4%) | 15.6 (34.1%) | 22.3 (50.4%) | 43.4 (39.8%) | 27.0 (21.6%) | 32.5 (29.8%) | 23.6 (124.7%) | 28.1 (8.8%) | 27.1 (29.1%) | 23.5 (20.9%) | 35.4 (52.9%) | 24.2 (58.6%) | 10.3 (241.0%) |
| Cycle 3 Day 1 (n=0,0,1,5,3,2,2,0,0,2,0,2,1) | | | 65.5 | 65.4 (31.4%) | 152 (25.5%) | 350 (45.4%) | 548 (48.3%) | | | 382 (2.2%) | | 198 (71.0%) | 134 |

## Area under the serum concentration-time curve from time zero to 14 days post dose (AUC0-14d) of KAZ954

| | |
|---|---|
| Description | PK parameters were calculated based on free KAZ954 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 3 Day 1 (C3D1): pre-dose, 1, 24, 72, 168, 240 and 360 hours after the end of the infusion. The duration of the infusion was 2 hours. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received KAZ954 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | **KAZ954 30 mg** | **KAZ954 50 mg** | **KAZ954 100 mg** | **KAZ954 150 mg** | **KAZ954 300 mg** | **KAZ954 600 mg** | **KAZ954 1200 mg** | **KAZ954 300 mg +** | **KAZ954 600 mg +** | **KAZ954 1200 mg +** | **KAZ954 300 mg +** | **KAZ954 600 mg +** | **KAZ954 600 mg +** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

| | | | | | | | | PDR001 400 mg | PDR001 400 mg | PDR001 400 mg | NIR178 160 mg | NIR178 160 mg | NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 3 | 10 | 5 | 4 | 8 | 2 | 3 | 7 | 4 | 4 | 3 |
| **Area under the serum concentration-time curve from time zero to 14 days post dose (AUC0-14d) of KAZ954** (units: hr*µg/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **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=3,4,3,10,5,4,8,2,3,7,4,4,3) | 684 (25.3%) | 1540 (30.0%) | 3380 (15.0%) | 5590 (44.4%) | 3240 (13.2%) | 3770 (31.9%) | 2550 (180.4%) | 3120 (37.8%) | 2790 (53.5%) | 2690 (17.2%) | 4370 (39.6%) | 3340 (35.1%) | 2380 (31.9%) |
| Cycle 3 Day 1 (n=0,0,1,5,3,2,2,0,0,2,0,2,1) | | | 12800 | 12100 (19.0%) | 29800 (16.1%) | 66000 (36.0%) | 75200 (33.6%) | | | 58900 (9.7%) | | 37200 (103.6%) | 25700 |

## Maximum observed serum concentration (Cmax) of PDR001

| | |
|---|---|
| Description | PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 3 Day 1 (C3D1): pre-dose, 1, 168, 336 and 672 hours after the end of the infusion. The duration of the infusion was 30 minutes. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received PDR001 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg + PDR001 400 mg** |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W |
| **Number of Participants Analyzed [units: participants]** | 1 | 2 | 3 |
| **Maximum observed serum concentration (Cmax) of PDR001** (units: µg/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** |
| Cycle 1 Day 1 (n=1,2,3) | 109 | 100 (41.6%) | 90.8 (2.9%) |
| Cycle 3 Day 1 (n=0,0,1) | | | 96.0 |

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

| | |
|---|---|
| Description | PK parameters were calculated based on PDR001 serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 3 Day 1 (C3D1): pre-dose, 1, 168, 336 and 672 hours after the end of the infusion. The duration of the infusion was 30 minutes. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received PDR001 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W |
| **Number of Participants Analyzed [units: participants]** | 1 | 2 | 3 |
| **Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of PDR001** (units: hr*µg/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** |
| Cycle 1 Day 1 (n=1,2,3) | 32300 | 25500 (48.3%) | 24100 (22.1%) |
| Cycle 3 Day 1 (n=0,0,1) | | | 30600 |

## Maximum observed plasma concentration (Cmax) of NIR178

| | |
|---|---|
| Description | PK parameters were calculated based on NIR178 plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 2 Day 1 (C2D1): pre-dose, 15 minutes, 1, 2, 4 and 6 hours after morning dose and 12 hours after evening dose. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |

| | | | |
|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 3 | 5 | 5 |
| **Maximum observed plasma concentration (Cmax) of NIR178** (units: ng/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** |
| Cycle 1 Day 1 (n=3,5,5) | 62.1 (280.9%) | 164 (1801.3%) | 441 (40.9%) |
| Cycle 2 Day 1 (n=3,4,5) | 538 (268.2%) | 444 (448.8%) | 1490 (83.7%) |

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

| | |
|---|---|
| Description | PK parameters were calculated based on NIR178 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 2 Day 1 (C2D1): pre-dose, 15 minutes, 1, 2, 4 and 6 hours after morning dose and 12 hours after evening dose. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 5 | 5 |
| **Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NIR178** (units: hr*ng/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** |
| Cycle 1 Day 1 (n=3,5,5) | 191 (142.3%) | 411 (4778.2%) | 1060 (48.1%) |
| Cycle 2 Day 1 (n=3,4,5) | 1660 (131.1%) | 1100 (423.7%) | 3560 (83.7%) |

## Maximum observed plasma concentration (Cmax) of NJI765 (NIR178 metabolite)

| | |
|---|---|
| Description | NJI765 is a NIR178 metabolite. PK parameters were calculated based on NJI765 plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 2 Day 1 (C2D1): pre-dose, 15 minutes, 1, 2, 4 and 6 hours after morning dose and 12 hours after evening dose. One cycle=28 days |
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | **KAZ954 300 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 160 mg** | **KAZ954 600 mg + NIR178 240 mg** |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 4 | 5 | 5 |
| **Maximum observed plasma concentration (Cmax) of NJI765 (NIR178 metabolite)** (units: ng/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** |
| Cycle 1 Day 1 (n=4,5,5) | 9.71 (107.1%) | 13.6 (63.6%) | 33.1 (30.1%) |
| Cycle 2 Day 1 (n=3,4,5) | 20.0 (440.0%) | 29.6 (48.9%) | 65.6 (54.1%) |

## Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NJI765 (NIR178 metabolite)

| | |
|---|---|
| Description | NJI765 is a NIR178 metabolite. PK parameters were calculated based on NJI765 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation. |
| Time Frame | Cycle 1 Day 1 (C1D1) and Cycle 2 Day 1 (C2D1): pre-dose, 15 minutes, 1, 2, 4 and 6 hours after morning dose and 12 hours after evening dose. One cycle=28 days |

| | |
|---|---|
| Analysis Population Description | Patients in the pharmacokinetic analysis set (PAS) who received NIR178 and had an available value for the outcome measure at each timepoint. PAS consisted of all patients who received one of the planned treatments and provided at least one primary PK parameter. |

| | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 4 | 5 | 5 |
| **Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of NJI765 (NIR178 metabolite)** (units: hr*ng/mL) | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** | **Geometric Mean (Geometric Coefficient of Variation)** |
| Cycle 1 Day 1 (n=4,5,5) | 29.7 (87.5%) | 35.5 (139.6%) | 97.2 (50.3%) |
| Cycle 2 Day 1 (n=3,4,5) | 73.4 (535.0%) | 102 (52.4%) | 242 (62.5%) |

## Number of participants with anti-KAZ954 antibodies

| | |
|---|---|
| Description | KAZ954 immunogenicity was evaluated in serum samples. Patient anti-drug antibodies (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: ADA-negative sample at baseline and at least 1 post-baseline sample, all of which are ADA-negative samples • Treatment-reduced ADA-positive: ADA-positive sample at baseline and at least 1 post-baseline sample, all of which are ADA-negative samples • Treatment-induced ADA-positive: ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive: ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample |
| Time Frame | Baseline (before first dose) and post-baseline (assessed throughout the treatment, up to approximately 48 weeks, 16 weeks and 20 weeks for KAZ954 single agent, KAZ954+PDR001 and KAZ954+NIR178, respectively) |
| Analysis Population Description | All patients who received at least 1 dose of KAZ954 and had a determinant baseline immunogenicity (IG) sample and at least 1 determinant post-baseline IG sample for assessing anti-KAZ954 antibodies. |

| | KAZ954 30 mg | KAZ954 50 mg | KAZ954 100 mg | KAZ954 150 mg | KAZ954 300 mg | KAZ954 600 mg | KAZ954 1200 mg | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg | KAZ954 300 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 160 mg | KAZ954 600 mg + NIR178 240 mg |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 9 | 4 | 3 | 8 | 3 | 4 | 6 |
| **Number of participants with anti-KAZ954 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)** | **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)** |
| ADA-negative at baseline | 3 (100%) | 4 (100%) | 4 (100%) | 11 (100%) | 5 (100%) | 6 (100%) | 9 (100%) | 4 (100%) | 3 (100%) | 8 (100%) | 3 (100%) | 4 (100%) | 6 (100%) |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ADA-positive at baseline | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| ADA-negative post-baseline | 3 (100%) | 3 (75%) | 4 (100%) | 9 (81.82%) | 5 (100%) | 6 (100%) | 9 (100%) | 4 (100%) | 3 (100%) | 8 (100%) | 3 (100%) | 3 (75%) | 5 (83.33%) |
| Treatment-reduced ADA-positive | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| Treatment-induced ADA-positive | 0 (%) | 1 (25%) | 0 (%) | 2 (18.18%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 1 (25%) | 1 (16.67%) |
| Treatment-boosted ADA-positive | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) | 0 (%) |

## Number of participants with anti-PDR001 antibodies

| | |
|---|---|
| Description | PDR001 immunogenicity was evaluated in serum samples. Patient anti-drug antibodies (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: ADA-negative sample at baseline and at least 1 post-baseline sample, all of which are ADA-negative samples • Treatment-reduced ADA-positive: ADA-positive sample at baseline and at least 1 post-baseline sample, all of which are ADA-negative samples • Treatment-induced ADA-positive: ADA-negative sample at baseline and at least 1 treatment-induced ADA-positive sample • Treatment-boosted ADA-positive: ADA-positive sample at baseline and at least 1 treatment-boosted ADA-positive sample |
| Time Frame | Baseline (before first dose) and post-baseline (assessed throughout the treatment, up to approximately 16 weeks) |
| Analysis Population Description | All patients who received at least 1 dose of PDR001 and had a determinant baseline immunogenicity (IG) sample and at least 1 determinant post-baseline IG sample for assessing anti-PDR001 antibodies. |

| | KAZ954 300 mg + PDR001 400 mg | KAZ954 600 mg + PDR001 400 mg | KAZ954 1200 mg + PDR001 400 mg |
|---|---|---|---|
| **Arm/Group Description** | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W |
| **Number of Participants Analyzed [units: participants]** | 5 | 1 | 7 |
| **Number of participants with anti-PDR001 antibodies** (units: participants) | **Count of Participants (Not Applicable)** | **Count of Participants (Not Applicable)** | **Count of Participants (Not Applicable)** |
| ADA-negative at baseline | 5 (100%) | 1 (100%) | 6 (85.71%) |
| ADA-positive at baseline | 0 (%) | 0 (%) | 1 (14.29%) |
| ADA-negative post-baseline | 5 (100%) | 1 (100%) | 5 (71.43%) |
| Treatment-reduced ADA-positive | 0 (%) | 0 (%) | 1 (14.29%) |
| Treatment-induced ADA-positive | 0 (%) | 0 (%) | 1 (14.29%) |
| Treatment-boosted ADA-positive | 0 (%) | 0 (%) | 0 (%) |

## Overall Response Rate (ORR) using RECIST v1.1 by PD-L1 expression

| | |
|---|---|
| Description | Programmed Death-Ligand 1 (PD-L1) expression was assessed centrally using the 22C3 PharmDx assay. PD-L1 expression levels were defined based on the tumor proportion score (TPS). The PD-L1 expression levels were categorized as high (TPS ≥ 50%), medium (TPS 1% - 49%) and low (TPS <1%) expressors. This record summarizes ORR using RECIST v1.1 by PD-L1 expression. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment and had a valid assessment for the outcome measure. |

| | KAZ954: PD-L1 Low | KAZ954: PD-L1 Medium | KAZ954: PD-L1 High | KAZ954+PDR001: PD-L1 Low | KAZ954+PDR001: PD-L1 Medium | KAZ954+NIR178: PD-L1 Low | KAZ954+NIR178: PD-L1 Medium |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | Treatment with KAZ954 single agent and PD-L1 expression levels low (TPS<1%) | Treatment with KAZ954 single agent and PD-L1 expression levels medium (TPS 1% - 49%) | Treatment with KAZ954 single agent and PD-L1 expression levels high (TPS>50%) | Treatment with KAZ954 in combination with spartalizumab and PD-L1 expression levels low (TPS<1%) | Treatment with KAZ954 in combination with spartalizumab and PD-L1 expression levels medium (TPS 1% - 49%) | Treatment with KAZ954 in combination with NIR178 and PD-L1 expression levels low (TPS<1%) | Treatment with KAZ954 in combination with NIR178 and PD-L1 expression levels medium (TPS 1% - 49%) |
| **Number of Participants Analyzed [units: participants]** | 26 | 5 | 2 | 11 | 5 | 10 | 2 |
| **Overall Response Rate (ORR) using RECIST v1.1 by PD-L1 expression** (units: percentage of participants) | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** |
| | 0 (0.0 to 10.9) | 0 (0.0 to 45.1) | 0 (0.0 to 77.6) | 0 (0.0 to 23.8) | 0 (0.0 to 45.1) | 0 (0.0 to 25.9) | 0 (0.0 to 77.6) |

## Overall Response Rate (ORR) using iRECIST by PD-L1 expression

| | |
|---|---|
| Description | PD-L1 expression was assessed centrally using the 22C3 PharmDx assay. PD-L1 expression levels were defined based on the tumor proportion score (TPS). The PD-L1 expression levels were categorized as high (TPS ≥ 50%), medium (TPS 1% - 49%) and low (TPS <1%) expressors. This record summarizes ORR using iRECIST by PD-L1 expression. |
| Time Frame | Up to approximately 48 weeks (KAZ954 single agent), 16 weeks (KAZ954+PDR001) and 20 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment and had a valid assessment for the outcome measure. |

| | KAZ954: PD-L1 Low | KAZ954: PD-L1 Medium | KAZ954: PD-L1 High | KAZ954+PDR001: PD-L1 Low | KAZ954+PDR001: PD-L1 Medium | KAZ954+NIR178: PD-L1 Low | KAZ954+NIR178: PD-L1 Medium |
|---|---|---|---|---|---|---|---|

| Arm/Group Description | Treatment with KAZ954 single agent and PD-L1 expression levels low (TPS<1%) | Treatment with KAZ954 single agent and PD-L1 expression levels medium (TPS 1% - 49%) | Treatment with KAZ954 single agent and PD-L1 expression levels high (TPS>50%) | Treatment with KAZ954 in combination with spartalizumab and PD-L1 expression levels low (TPS<1%) | Treatment with KAZ954 in combination with spartalizumab and PD-L1 expression levels medium (TPS 1% - 49%) | Treatment with KAZ954 in combination with NIR178 and PD-L1 expression levels low (TPS<1%) | Treatment with KAZ954 in combination with NIR178 and PD-L1 expression levels medium (TPS 1% - 49%) |
|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 26 | 5 | 2 | 11 | 5 | 10 | 2 |
| **Overall Response Rate (ORR) using iRECIST by PD-L1 expression** (units: percentage of participants) | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** | **Number (90% Confidence Interval)** |
| | 0 (0.0 to 10.9) | 0 (0.0 to 45.1) | 0 (0.0 to 77.6) | 0 (0.0 to 23.8) | 0 (0.0 to 45.1) | 0 (0.0 to 25.9) | 0 (0.0 to 77.6) |

## Progression Free Survival (PFS) using RECIST v1.1 by PD-L1 expression

| | |
|---|---|
| Description | PD-L1 expression was assessed centrally using the 22C3 PharmDx assay. PD-L1 expression levels were defined based on the tumor proportion score (TPS). The PD-L1 expression levels were categorized as high (TPS ≥ 50%), medium (TPS 1% - 49%) and low (TPS <1%) expressors. This record summarizes PFS using RECIST v1.1 by PD-L1 expression. |
| Time Frame | Up to approximately 52 weeks (KAZ954 single agent), 20 weeks (KAZ954+PDR001) and 24 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment and had a valid assessment for the outcome measure. |

| | KAZ954: PD-L1 Low | KAZ954: PD-L1 Medium | KAZ954: PD-L1 High | KAZ954+PDR001: PD-L1 Low | KAZ954+PDR001: PD-L1 Medium | KAZ954+NIR178: PD-L1 Low | KAZ954+NIR178: PD-L1 Medium |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | Treatment with KAZ954 single agent | Treatment with KAZ954 single agent | Treatment with KAZ954 single agent | Treatment with KAZ954 in combination with | Treatment with KAZ954 in combination with | Treatment with KAZ954 in combination with | Treatment with KAZ954 in combination with |

| | and PD-L1 expression levels low (TPS<1%) | and PD-L1 expression levels medium (TPS 1% - 49%) | and PD-L1 expression levels high (TPS>50%) | spartalizumab and PD-L1 expression levels low (TPS<1%) | spartalizumab and PD-L1 expression levels medium (TPS 1% - 49%) | NIR178 and PD-L1 expression levels low (TPS<1%) | NIR178 and PD-L1 expression levels medium (TPS 1% - 49%) |
|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 26 | 5 | 2 | 11 | 5 | 10 | 2 |
| **Progression Free Survival (PFS) using RECIST v1.1 by PD-L1 expression** (units: months) | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** |
| | 1.6 (1.5 to 1.9) | 1.8 (0.7 to NA)[1] | 1.5 (1.2 to NA)[1] | 1.8 (0.2 to 2.0) | 1.9 (1.5 to NA)[1] | 1.7 (1.4 to 3.5) | 1.1 (0.5 to NA)[1] |

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

## Progression Free Survival (PFS) using iRECIST by PD-L1 expression

| | |
|---|---|
| Description | PD-L1 expression was assessed centrally using the 22C3 PharmDx assay. PD-L1 expression levels were defined based on the tumor proportion score (TPS). The PD-L1 expression levels were categorized as high (TPS ≥ 50%), medium (TPS 1% - 49%) and low (TPS <1%) expressors. This record summarizes PFS using iRECIST by PD-L1 expression. |
| Time Frame | Up to approximately 52 weeks (KAZ954 single agent), 20 weeks (KAZ954+PDR001) and 24 weeks (KAZ954+NIR178) |
| Analysis Population Description | All patients who received at least one dose of study treatment and had a valid assessment for the outcome measure. |

| | **KAZ954: PD-L1 Low** | **KAZ954: PD-L1 Medium** | **KAZ954: PD-L1 High** | **KAZ954+PDR001: PD-L1 Low** | **KAZ954+PDR001: PD-L1 Medium** | **KAZ954+NIR178: PD-L1 Low** | **KAZ954+NIR178: PD-L1 Medium** |
|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | Treatment with KAZ954 single agent and PD-L1 expression | Treatment with KAZ954 single agent and PD-L1 expression levels | Treatment with KAZ954 single agent and PD-L1 expression | Treatment with KAZ954 in combination with spartalizumab and PD-L1 expression | Treatment with KAZ954 in combination with spartalizumab and PD-L1 expression | Treatment with KAZ954 in combination with NIR178 and PD-L1 expression | Treatment with KAZ954 in combination with NIR178 and PD-L1 expression |

| | levels low (TPS<1%) | medium (TPS 1% - 49%) | levels high (TPS>50%) | levels low (TPS<1%) | levels medium (TPS 1% - 49%) | levels low (TPS<1%) | levels medium (TPS 1% - 49%) |
|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 26 | 5 | 2 | 11 | 5 | 10 | 2 |
| **Progression Free Survival (PFS) using iRECIST by PD-L1 expression** (units: months) | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** | **Median (90% Confidence Interval)** |
| | 1.7 (1.3 to 2.4) | 1.8 (0.7 to NA)[1] | 1.5 (1.2 to NA)[1] | 1.9 (0.8 to 2.1) | 1.9 (1.5 to NA)[1] | 1.7 (1.4 to 2.2) | 1.1 (0.5 to NA)[1] |

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

# Post-Hoc Outcome Result(s)

## All-Collected Deaths

| | |
|---|---|
| Description | On-treatment and post-treatment safety follow-up (FU) deaths were collected from first dose of study medication to 90 days after last dose of KAZ954 and KAZ954+NIR178 and 150 days after last dose of KAZ954+PDR001. Survival FU deaths were collected from 91 days after last dose of KAZ954 and KAZ954+NIR178 and 151 days after last dose of NIR178+PDR001 until end of study. All deaths refer to the sum of on-treatment and post-treatment safety FU deaths plus survival FU deaths. |
| Time Frame | On-treatment and safety FU deaths: up to approximately 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). Survival FU deaths: up to approximately 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001) |
| Analysis Population Description | All patients who received at least one dose of study treatment. |

| **KAZ954 30 mg** | **KAZ954 50 mg** | **KAZ954 100 mg** | **KAZ954 150 mg** | **KAZ954 300 mg** | **KAZ954 600 mg** | **KAZ954 1200 mg** | **KAZ954 300 mg + PDR001 400 mg** | **KAZ954 600 mg + PDR001 400 mg** | **KAZ954 1200 mg +** | **KAZ954 300 mg +** | **KAZ954 600 mg +** | **KAZ954 600 mg +** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

| Arm/Group Description | KAZ954 30 mg IV Q2W | KAZ954 50 mg IV Q2W | KAZ954 100 mg IV Q2W | KAZ954 150 mg IV Q2W | KAZ954 300 mg IV Q2W | KAZ954 600 mg IV Q2W | KAZ954 1200 mg IV Q2W | KAZ954 300 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | KAZ954 600 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | **PDR001 400 mg** KAZ954 1200 mg IV Q2W in combination with spartalizumab 400 mg IV Q4W | **NIR178 160 mg** KAZ954 300 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | **NIR178 160 mg** KAZ954 600 mg IV Q2W in combination with NIR178 160 mg oral b.i.d. | **NIR178 240 mg** KAZ954 600 mg IV Q2W in combination with NIR178 240 mg oral b.i.d. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Number of Participants Analyzed [units: participants]** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 |
| **All-Collected Deaths** (units: participants) | | | | | | | | | | | | | |
| On-treatment and post-treatment safety FU deaths (n=3,4,4,11,5,6,10,5,4,9,4,6,6) | 1 | 2 | 1 | 1 | 1 | 2 | 7 | 2 | 1 | 5 | 2 | 2 | 3 |
| Survival FU deaths (n=2,2,3,10,4,4,3,3,3,4,2,4,3) | 1 | 0 | 1 | 4 | 0 | 1 | 0 | 0 | 0 | 2 | 1 | 2 | 0 |
| All deaths (n=3,4,4,11,5,6,10,5,4,9,4,6,6) | 2 | 2 | 2 | 5 | 1 | 3 | 7 | 2 | 1 | 7 | 3 | 4 | 3 |

## Safety Results

| | |
|---|---|
| **Time Frame** | On- and post-treatment safety FU: from first dose of study medication to 90 days after last dose of KAZ954 and KAZ954+NIR178 and 150 days after last dose of KAZ954+PDR001, up to approx. 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). Deaths in survival period: from 91 days after last dose of KAZ954 and KAZ954+NIR178 and 151 days after last dose of NIR178+PDR001 until end of study, up to approx. 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). |
| **Additional Description** | Deaths in the survival period are not considered Adverse Events (AEs). No AEs were collected in the survival period. |
| **Source Vocabulary for Table Default** | MedDRA (26.1) |
| **Collection Approach for Table Default** | Systematic Assessment |

## All-Cause Mortality

| | **KAZ 954 30 mg N = 3** | **KAZ 954 50 mg N = 4** | **KAZ 954 100 mg N = 4** | **KAZ 954 150 mg N = 11** | **KAZ 954 300 mg N = 5** | **KAZ 954 600 mg N = 6** | **KAZ 954 1200 mg N = 10** | **KAZ954 300 mg + PDR001 400 mg N = 5** | **KAZ954 600 mg + PDR001 400 mg N = 4** | **KAZ954 1200 mg + PDR001 400 mg N = 9** | **KAZ954 300 mg + NIR178 160 mg N = 4** | **KAZ954 600 mg + NIR178 160 mg N = 6** | **KAZ954 600 mg + NIR178 240 mg N = 6** | **All patients_ On- and post-treatment safety FU N = 77** | **All patients_ Survival FU N = 47** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | Safety data up to 90 days after last dose of | Safety data up to 90 days after last dose of | Safety data up to 90 days after last dose of | Safety data up to 90 days after last dose of | Safety data up to 90 days after last dose of | Safety data up to 90 days after last dose of | Safety data up to 90 days after last dose of | Safety data up to 150 days after last dose of KAZ954+ PDR001 | Safety data up to 150 days after last dose of KAZ954+ PDR001 | Safety data up to 150 days after last dose of KAZ954+ PDR001 | Safety data up to 90 days after last dose of KAZ954+ NIR178 | Safety data up to 90 days after last dose of KAZ954+ NIR178 | Safety data up to 90 days after last dose of KAZ954+ NIR178 | Safety data up to 90 days after last dose of KAZ954 and KAZ954+ NIR178 and 150 days after last dose | Deaths collected from 91 days after last dose of KAZ954 and KAZ954+ NIR178 and 151 days after |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | KAZ 954 | KAZ 954 | KAZ 954 | KAZ 954 | KAZ 954 | KAZ 954 | KAZ 954 | | | | | | | of KAZ954+ PDR001 | last dose of NIR178+ PDR001 until end of study |
| **Total Number Affected** | 1 | 2 | 1 | 1 | 1 | 2 | 7 | 2 | 1 | 5 | 2 | 2 | 3 | 30 | 12 |
| **Total Number At Risk** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 | 47 |

## Serious Adverse Events

| | |
|---|---|
| **Time Frame** | On- and post-treatment safety FU: from first dose of study medication to 90 days after last dose of KAZ954 and KAZ954+NIR178 and 150 days after last dose of KAZ954+PDR001, up to approx. 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). Deaths in survival period: from 91 days after last dose of KAZ954 and KAZ954+NIR178 and 151 days after last dose of NIR178+PDR001 until end of study, up to approx. 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). |
| **Additional Description** | Deaths in the survival period are not considered Adverse Events (AEs). No AEs were collected in the survival period. |
| **Source Vocabulary for Table Default** | MedDRA (26.1) |
| **Collection Approach for Table Default** | Systematic Assessment |

| | KAZ 954 30 mg N = 3 | KAZ 954 50 mg N = 4 | KAZ 954 100 mg N = 4 | KAZ 954 150 mg N = 11 | KAZ 954 300 mg N = 5 | KAZ 954 600 mg N = 6 | KAZ 954 1200 mg N = 10 | KAZ954 300 mg + PDR001 400 mg N = 5 | KAZ954 600 mg + PDR001 400 mg N = 4 | KAZ954 1200 mg + PDR001 400 mg N = 9 | KAZ95 4 300 mg + NIR178 160 mg N = 4 | KAZ95 4 600 mg + NIR178 160 mg N = 6 | KAZ95 4 600 mg + NIR178 240 mg N = 6 | All patients _On- and post- treatment safety FU N = 77 | All patients _Survival FU N = 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 90 days after last dose of KAZ 954 | Safety data up to 150 days after last dose of KAZ954 +PDR001 | Safety data up to 150 days after last dose of KAZ954 +PDR001 | Safety data up to 150 days after last dose of KAZ954 +PDR001 | Safety data up to 90 days after last dose of KAZ954 +NIR178 | Safety data up to 90 days after last dose of KAZ954 +NIR178 | Safety data up to 90 days after last dose of KAZ954 +NIR178 | Safety data up to 90 days after last dose of KAZ954 and KAZ954 +NIR178 and 150 days after last dose of KAZ954 +PDR001 | Deaths collected from 91 days after last dose of KAZ954 and KAZ954 +NIR178 and 151 days after last dose of NIR178+ PDR001 until end of study |
| **Total # Affected by any Serious Adverse Event** | 2 | 1 | 4 | 6 | 3 | 3 | 6 | 4 | 2 | 4 | 3 | 4 | 3 | 45 | 0 |
| **Total # at Risk by any Serious Adverse Event** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 | 0 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Blood and lymphatic system disorders** | | | | | | | | | | | | | | |
| Anaemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Thrombocytopenia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Cardiac disorders** | | | | | | | | | | | | | | |
| Myocardial infarction | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Myocarditis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Ear and labyrinth disorders** | | | | | | | | | | | | | | |
| Vertigo | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Gastrointestinal disorders** | | | | | | | | | | | | | | |
| Abdominal pain | 1 (33.33%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 1 (25.00%) | 1 (11.11%) | 2 (50.00%) | 1 (16.67%) | 0 (0.00%) | 8 (10.39%) |
| Abdominal pain upper | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| 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%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| 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%) | 0 (0.00%) | 1 (1.30%) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Large intestinal obstruction | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| 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 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Rectal haemorrhage | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| Upper gastrointestinal haemorrhage | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Vomiting | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **General disorders and administration site conditions** | | | | | | | | | | | | | | |
| Fatigue | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Pyrexia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 3 (3.90%) |
| **Hepatobiliary disorders** | | | | | | | | | | | | | | |
| Cholangitis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hypertransaminasaemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Immune system disorders** | | | | | | | | | | | | | |
| Cytokine release syndrome | 1 (33.33%) | 0 (0.00%) | 3 (75.00%) | 2 (18.18%) | 1 (20.00%) | 2 (33.33%) | 0 (0.00%) | 2 (40.00%) | 1 (25.00%) | 2 (22.22%) | 0 (0.00%) | 1 (16.67%) | 3 (50.00%) | 18 (23.38%) |
| **Infections and infestations** | | | | | | | | | | | | | |
| Bacteraemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Cellulitis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |
| Device related infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Sepsis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (40.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 3 (3.90%) |
| Urinary tract infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Injury, poisoning and procedural complications** | | | | | | | | | | | | | |
| Accidental overdose | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cardiac procedure complication | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Metabolism and nutrition disorders** | | | | | | | | | | | | | | |
| Decreased appetite | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Hyperglycaemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| 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%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 2 (2.60%) |
| **Musculoskeletal and connective tissue disorders** | | | | | | | | | | | | | | |
| Back pain | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |
| Pain in extremity | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| Pathological fracture | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Neoplasms benign, malignant and unspecified (incl cysts and polyps)** | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tumour thrombosis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Nervous system disorders** | | | | | | | | | | | | | | |
| Neuritis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Psychiatric disorders** | | | | | | | | | | | | | | |
| Delirium | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Insomnia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Mental status changes | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Reproductive system and breast disorders** | | | | | | | | | | | | | | |
| Female genital tract fistula | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| **Respiratory, thoracic and mediastinal disorders** | | | | | | | | | | | | | | |
| Dyspnoea | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pleural effusion | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Pneumothorax | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Pulmonary embolism | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (3.90%) |

## Other (Not Including Serious) Adverse Events

| | |
|---|---|
| **Time Frame** | On- and post-treatment safety FU: from first dose of study medication to 90 days after last dose of KAZ954 and KAZ954+NIR178 and 150 days after last dose of KAZ954+PDR001, up to approx. 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). Deaths in survival period: from 91 days after last dose of KAZ954 and KAZ954+NIR178 and 151 days after last dose of NIR178+PDR001 until end of study, up to approx. 61 weeks (KAZ954), 37 weeks (KAZ954+NIR178) and 33 weeks (KAZ954+PDR001). |
| **Additional Description** | Deaths in the survival period are not considered Adverse Events (AEs). No AEs were collected in the survival period. |
| **Source Vocabulary for Table Default** | MedDRA (26.1) |
| **Collection Approach for Table Default** | Systematic Assessment |
| **Frequent Event Reporting Threshold** | 5% |

| | KAZ954 30 mg N = 3 | KAZ954 50 mg N = 4 | KAZ954 100 mg N = 4 | KAZ954 150 mg N = 11 | KAZ954 300 mg N = 5 | KAZ954 600 mg N = 6 | KAZ954 1200 mg N = 10 | KAZ954 300 mg + PDR001 400 mg N = 5 | KAZ954 600 mg + PDR001 400 mg N = 4 | KAZ954 1200 mg + PDR001 400 mg N = 9 | KAZ954 300 mg + NIR178 160 mg N = 4 | KAZ954 600 mg + NIR178 160 mg N = 6 | KAZ954 600 mg + NIR178 240 mg N = 6 | All patients_On-and post-treatment safety FU N = 77 | All patients_Survival FU N = 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Arm/Group Description** | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 90 days after last dose of KAZ954 | Safety data up to 150 days after last dose of KAZ954 +PDR001 | Safety data up to 150 days after last dose of KAZ954 +PDR001 | Safety data up to 150 days after last dose of KAZ954 +PDR001 | Safety data up to 90 days after last dose of KAZ954 +NIR178 | Safety data up to 90 days after last dose of KAZ954 +NIR178 | Safety data up to 90 days after last dose of KAZ954 +NIR178 | Safety data up to 90 days after last dose of KAZ954 and KAZ954 +NIR178 and 150 days after last dose of KAZ954 +PDR001 | Deaths collected from 91 days after last dose of KAZ954 and KAZ954 +NIR178 and 151 days after last dose of NIR178+ PDR001 until end of study |
| **Total # Affected by any Other Adverse Event** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 | 0 |
| **Total # at Risk by any Other Adverse Event** | 3 | 4 | 4 | 11 | 5 | 6 | 10 | 5 | 4 | 9 | 4 | 6 | 6 | 77 | 0 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Blood and lymphatic system disorders** | | | | | | | | | | | | | |
| Anaemia | 1 (33.33%) | 2 (50.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 1 (16.67%) | 1 (10.00%) | 1 (20.00%) | 1 (25.00%) | 2 (22.22%) | 0 (0.00%) | 2 (33.33%) | 0 (0.00%) | 12 (15.58%) |
| Disseminated intravascular coagulation | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Leukocytosis | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Lymphopenia | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 2 (40.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 1 (16.67%) | 1 (16.67%) | 7 (9.09%) |
| Thrombocytopenia | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| **Cardiac disorders** | | | | | | | | | | | | | |
| Arrhythmia | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| Atrial fibrillation | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Myocarditis | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Sinus tachycardia | 0 (0.0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tachycardia | 2 (66.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| **Ear and labyrinth disorders** | | | | | | | | | | | | | | |
| Vertigo | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Endocrine disorders** | | | | | | | | | | | | | | |
| Hyperthyroidism | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |
| Thyroiditis | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Eye disorders** | | | | | | | | | | | | | | |
| Altered visual depth perception | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Conjunctival haemorrhage | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Diplopia | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Dry eye | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Vision blurred | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Gastrointestinal disorders** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Abdominal discomfort | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Abdominal distension | 1 (33.33%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 1 (11.11%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 6 (7.79%) |
| Abdominal pain | 1 (33.33%) | 0 (0.00%) | 0 (0.00%) | 4 (36.36%) | 1 (20.00%) | 1 (16.67%) | 3 (30.00%) | 0 (0.00%) | 0 (0.00%) | 3 (33.33%) | 2 (50.00%) | 1 (16.67%) | 0 (0.00%) | 16 (20.78%) |
| Abdominal pain upper | 1 (33.33%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 1 (20.00%) | 1 (25.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 6 (7.79%) |
| Ascites | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 4 (5.19%) |
| Constipation | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 3 (27.27%) | 1 (20.00%) | 2 (33.33%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 1 (25.00%) | 2 (33.33%) | 2 (33.33%) | 14 (18.18%) |
| Defaecation urgency | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |
| Diarrhoea | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (27.27%) | 0 (0.00%) | 1 (16.67%) | 2 (20.00%) | 3 (60.00%) | 1 (25.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 2 (33.33%) | 13 (16.88%) |
| Dry mouth | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 4 (5.19%) |
| Dyspepsia | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (3.90%) |
| Dysphagia | 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%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Flatulence | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Impaired gastric emptying | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 1 (11.11 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 2 (2.60 %) |
| Melaena | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Mesenteric vein thrombosis | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Nausea | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 3 (60 .00% ) | 1 (16 .67% ) | 5 (50 .00% ) | 1 (20.00 %) | 1 (25.00 %) | 1 (11.11 %) | 1 (25.00 %) | 3 (50.00 %) | 5 (83.33 %) | 22 (28.5 7%) |
| Proctalgia | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 1 (16 .67% ) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 3 (3.90 %) |
| Rectal discharge | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 1 (1.30 %) |
| Stomatitis | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 3 (3.90 %) |
| Varices oesophageal | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Vomiting | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 2 (18 .18% ) | 1 (20 .00% ) | 1 (16 .67% ) | 3 (30 .00% ) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 4 (66.67 %) | 14 (18.1 8%) |
| **General disorders and administration site conditions** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Asthenia | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 3 (27 .27% ) | 1 (20 .00% ) | 2 (33 .33% ) | 4 (40 .00% ) | 1 (20.00 %) | 0 (0.00 %) | 2 (22.22 %) | 1 (25.00 %) | 2 (33.33 %) | 2 (33.33 %) | 19 (24.6 8%) |
| Chest discomfo rt | 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 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Chest pain | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Chills | 2 (66. 67%) | 0 (0. 00%) | 1 (25 .00% ) | 2 (18 .18% ) | 3 (60 .00% ) | 2 (33 .33% ) | 3 (30 .00% ) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 3 (50.00 %) | 18 (23.3 8%) |
| Extravas ation | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Fatigue | 1 (33. 33%) | 1 (25 .00% ) | 0 (0. 00%) | 5 (45 .45% ) | 3 (60 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 1 (20.00 %) | 0 (0.00 %) | 1 (11.11 %) | 1 (25.00 %) | 2 (33.33 %) | 1 (16.67 %) | 16 (20.7 8%) |
| Feeling hot | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 1 (11.11 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Influenza like illness | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 1 (1.30 %) |
| Localise d oedema | 1 (33. 33%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 2 (2.60 %) |
| Non-cardiac chest pain | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 1 (1.30 %) |
| Oedema | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Oedema peripher al | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 4 (5.19 %) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pain | 0 (0.0 0%) | 0 (0. 00%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 4 (5.19 %) |
| Pyrexia | 3 (10 0.00 %) | 1 (25 .00% ) | 1 (25 .00% ) | 0 (0. 00%) | 1 (20 .00% ) | 4 (66 .67% ) | 2 (20 .00% ) | 1 (20.00 %) | 1 (25.00 %) | 1 (11.11 %) | 2 (50.00 %) | 2 (33.33 %) | 2 (33.33 %) | 21 (27.2 7%) |
| **Hepatobiliary disorders** | | | | | | | | | | | | | | |
| Biliary obstruction | 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 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Cholecystitis | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (16 .67% ) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Cholestasis | 0 (0.0 0%) | 0 (0. 00%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Hepatic function abnormal | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 2 (2.60 %) |
| Hyperbilirubinaemia | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 2 (18 .18% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 1 (11.11 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 4 (5.19 %) |
| **Immune system disorders** | | | | | | | | | | | | | | |
| Cytokine release syndrome | 0 (0.0 0%) | 1 (25 .00% ) | 1 (25 .00% ) | 1 (9. 09%) | 0 (0. 00%) | 1 (16 .67% ) | 2 (20 .00% ) | 1 (20.00 %) | 1 (25.00 %) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 2 (33.33 %) | 11 (14.2 9%) |
| Hypersensitivity | 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 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Seasonal allergy | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 1 (11.11 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| **Infections and infestations** | | | | | | | | | | | | | | |
| Bacteraemia | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 1 (1.30 %) |
| Bronchitis | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Catheter site infection | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Conjunctivitis | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| COVID-19 | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 1 (25.00 %) | 1 (11.11 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 3 (3.90 %) |
| Cystitis | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Device related infection | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (16 .67% ) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Enterocolitis infectious | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Herpes zoster | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Rash pustular | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sialoadenitis | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Upper respiratory tract infection | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Urinary tract infection | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (16.67%) | 4 (5.19%) |
| **Injury, poisoning and procedural complications** | | | | | | | | | | | | | | |
| Fall | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Infusion related reaction | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 2 (40.00%) | 1 (25.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 1 (16.67%) | 7 (9.09%) |
| Post procedural inflammation | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Procedural nausea | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Procedural pain | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Investigations** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Alanine aminotransferase increased | 2 (66.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 4 (40.00%) | 0 (0.00%) | 2 (50.00%) | 2 (22.22%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 11 (14.29%) |
| Amylase increased | 0 (0.00%) | 0 (0.00%) | 2 (50.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (3.90%) |
| Aspartate aminotransferase increased | 2 (66.67%) | 1 (25.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 1 (16.67%) | 4 (40.00%) | 0 (0.00%) | 1 (25.00%) | 2 (22.22%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 13 (16.88%) |
| Blood alkaline phosphatase increased | 2 (66.67%) | 1 (25.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 1 (16.67%) | 1 (10.00%) | 1 (20.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 2 (33.33%) | 0 (0.00%) | 11 (14.29%) |
| Blood bilirubin increased | 2 (66.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (20.00%) | 0 (0.00%) | 1 (25.00%) | 1 (11.11%) | 1 (25.00%) | 1 (16.67%) | 2 (33.33%) | 10 (12.99%) |
| Blood cholesterol increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| Blood creatine phosphokinase increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Blood creatinine increased | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 3 (3.90%) |
| Blood lactate dehydrogenase increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Clostridium test positive | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| C-reactive protein increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (33.33%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Gamma-glutamyltransferase increased | 2 (66.67%) | 1 (25.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 2 (33.33%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 2 (22.22%) | 0 (0.00%) | 2 (33.33%) | 0 (0.00%) | 12 (15.58%) |
| International normalised ratio increased | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Lipase increased | 0 (0.00%) | 2 (50.00%) | 1 (25.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 6 (7.79%) |
| Lymphocyte count | 2 (66.67%) | 2 (50.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 1 (11.11%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 7 (9.09%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| decreased | | | | | | | | | | | | | | |
| Pancreatic enzymes decreased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Platelet count decreased | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Transaminases increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| Weight decreased | 2 (66.67%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 5 (6.49%) |
| Weight increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| **Metabolism and nutrition disorders** | | | | | | | | | | | | | | |
| Decreased appetite | 2 (66.67%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 1 (20.00%) | 1 (16.67%) | 3 (30.00%) | 1 (20.00%) | 1 (25.00%) | 1 (11.11%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 13 (16.88%) |
| Dehydration | 1 (33.33%) | 0 (0.00%) | 0 (0.00%) | 3 (27.27%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 5 (6.49%) |
| Hyperamylasaemia | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hypercalcaemia | 0 (0.0 0%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Hyperglycaemia | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Hyperkalaemia | 0 (0.0 0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Hyperlipasaemia | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Hyperphosphataemia | 0 (0.0 0%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Hyperuricaemia | 0 (0.0 0%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Hypoalbuminaemia | 2 (66.67%) | 2 (50.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 5 (6.49%) |
| Hypocalcaemia | 0 (0.0 0%) | 2 (50.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (3.90%) |
| Hypokalaemia | 0 (0.0 0%) | 1 (25.00%) | 0 (0.00%) | 3 (27.27%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 5 (6.49%) |
| Hypomagnesaemia | 0 (0.0 0%) | 1 (25.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 3 (50.00%) | 6 (7.79%) |
| Hyponatraemia | 2 (66.67%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 6 (7.79%) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hypophosphataemia | 0 (0.0 0%) | 0 (0. 00%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 1 (11.11 %) | 1 (25.00 %) | 0 (0.00 %) | 1 (16.67 %) | 4 (5.19 %) |
| Polydipsia | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 2 (2.60 %) |
| **Musculoskeletal and connective tissue disorders** | | | | | | | | | | | | | | |
| Arthralgia | 2 (66. 67%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 1 (25.00 %) | 2 (22.22 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 6 (7.79 %) |
| Back pain | 1 (33. 33%) | 0 (0. 00%) | 0 (0. 00%) | 2 (18 .18% ) | 2 (40 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 1 (25.00 %) | 2 (22.22 %) | 1 (25.00 %) | 0 (0.00 %) | 0 (0.00 %) | 9 (11.69 %) |
| Flank pain | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 1 (1.30 %) |
| Muscle spasms | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 1 (16.67 %) | 3 (3.90 %) |
| Muscular weakness | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 2 (2.60 %) |
| Musculoskeletal chest pain | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 1 (1.30 %) |
| Myalgia | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 1 (9. 09%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 4 (5.19 %) |
| Neck pain | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pain in extremity | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 1 (16 .67% ) | 0 (0. 00%) | 1 (20.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 4 (5.19 %) |
| Temporo mandibul ar joint syndrom e | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 1 (11.11 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| **Neoplasm s benign, malignant and unspecifie d (incl cysts and polyps)** | | | | | | | | | | | | | | |
| Melanoc ytic naevus | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Metastas es to central nervous system | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| **Nervous system disorders** | | | | | | | | | | | | | | |
| Dizzines s | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 1 (16 .67% ) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 4 (5.19 %) |
| Dysgeusi a | 2 (66. 67%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 2 (2.60 %) |
| Headach e | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 3 (27 .27% ) | 1 (20 .00% ) | 0 (0. 00%) | 4 (40 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (25.00 %) | 1 (16.67 %) | 3 (50.00 %) | 13 (16.8 8%) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hypoaesthesia | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Lethargy | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Myoclonus | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Neuropathy peripheral | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Ophthalmic migraine | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 1 (1.30 %) |
| Paraesthesia | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Peripheral sensory neuropathy | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (25.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Post herpetic neuralgia | 0 (0.0 0%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Restless legs syndrome | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 1 (1.30 %) |
| Sinus headache | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Somnolence | 0 (0.0 0%) | 2 (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 %) | 0 (0.00 %) | 2 (2.60 %) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Syncope | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 1 (1.30 %) |
| Tension headach e | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 0 (0.00 %) | 1 (1.30 %) |
| **Psychiatri c disorders** | | | | | | | | | | | | | | |
| Hallucina tion, auditory | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| Insomnia | 1 (33. 33%) | 1 (25 .00% ) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (20.00 %) | 0 (0.00 %) | 1 (11.11 %) | 0 (0.00 %) | 3 (50.00 %) | 0 (0.00 %) | 7 (9.09 %) |
| Restless ness | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 1 (10 .00% ) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| **Renal and urinary disorders** | | | | | | | | | | | | | | |
| Acute kidney injury | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (16.67 %) | 1 (1.30 %) |
| Chromat uria | 2 (66. 67%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 2 (2.60 %) |
| Proteinur ia | 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 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |
| **Reproduct ive system and breast disorders** | | | | | | | | | | | | | | |
| Breast pain | 0 (0.0 0%) | 0 (0. 00%) | 0 (0. 00%) | 1 (9. 09%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0. 00%) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 0 (0.00 %) | 1 (1.30 %) |

| **Respiratory, thoracic and mediastinal disorders** | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cough | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (11.11%) | 1 (25.00%) | 1 (16.67%) | 0 (0.00%) | 4 (5.19%) |
| Dyspnoea | 1 (33.33%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (20.00%) | 1 (25.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 1 (16.67%) | 8 (10.39%) |
| 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%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 2 (2.60%) |
| Epistaxis | 0 (0.00%) | 1 (25.00%) | 1 (25.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 3 (3.90%) |
| 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 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| 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%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |
| Pleural 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%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 2 (2.60%) |
| Productive cough | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Rhinorrhoea | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Sputum increased | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Skin and subcutaneous tissue disorders** | | | | | | | | | | | | | | |
| Dry skin | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Nail disorder | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 1 (1.30%) |
| Pruritus | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (9.09%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Rash | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| Rash maculo-papular | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 1 (11.11%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (2.60%) |
| Urticaria | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 0 (0.00%) | 1 (1.30%) |
| **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%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (25.00%) | 0 (0.00%) | 0 (0.00%) | 1 (1.30%) |
| 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%) | 1 (16.67%) | 2 (2.60%) |
| Hot flush | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (20.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 1 (16.67%) | 2 (2.60%) |
| Hypertension | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (40.00%) | 1 (16.67%) | 1 (10.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 4 (5.19%) |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hypotension | 1 (33.33%) | 0 (0.00%) | 0 (0.00%) | 2 (18.18%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 0 (0.00%) | 2 (22.22%) | 0 (0.00%) | 1 (16.67%) | 1 (16.67%) | 7 (9.09%) |

## Conclusion:

- The maximum tolerated dose/recommended dose for expansion (MTD/RDEs) were not reached prior to study termination. The maximum dose of KAZ954 administered was 1200 mg in the KAZ954 single agent and the KAZ954 + PDR001 groups and 600 mg in the KAZ954 + NIR178 group.
- ORR by RECIST, iRECIST and considering expression of PD-L1 was 0%. The best overall response in each group was stable disease. The KAZ954 single agent group had the highest DCR (20.9%). However, the results should be interpreted with caution considering the small sample size and large CI in each group.
- The incidence of treatment induced KAZ954 ADA-positive samples during the course of the study was low, 3 patients treated in the KAZ954 single agent group and 2 patients in the KAZ954 + NIR178 group. The incidence of treatment induced PDR001 ADA-positive samples during the course of the study was low, 1 patient in the KAZ954 + PDR001 group.
- Safety and tolerability in this study were acceptable and would not preclude further development of KAZ954 as a single agent or in combination with PDR001 or NIR178.

## Date of Clinical Trial Report

26-Jun-2024