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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

TNO155, spartalizumab (PDR001) and ribociclib (LEE011)

Trial Indication(s)

Advanced solid tumors

Protocol Number

CTNO155B12101

Protocol Title

A Phase Ib, open-label, multi-center study to characterize the safety, tolerability, and preliminary efficacy of TNO155 in combination with spartalizumab or ribociclib in selected malignancies

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1 (TNO155), Phase 3 (spartalizumab) and Phase 4 (ribociclib)

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Study Start/End Dates

Study Start Date: July 30, 2019 (Actual)

Primary Completion Date: January 15, 2024 (Actual)

Study Completion Date: January 15, 2024 (Actual)

Reason for Termination (If applicable)

The sponsor decided to halt the study enrollment on 15-Mar-2023 for business reasons. Importantly, this decision was not based on any safety/tolerability concerns for either of the combinations in the explored indications. Following the study enrollment halt during the escalation dose part of the study, the expansion part of the study was not initiated. The patients were allowed to continue their treatment as per protocol.

Study Design/Methodology

This study was a Phase Ib, multi-center, open-label study with a dose escalation part followed by a dose expansion part in adult patients with advanced solid tumors.

The study design included a dose escalation part and a dose expansion part. In the first part of the study, dose escalation, patients received oral TNO155 in combination with intravenous (i.v.) spartalizumab, or oral TNO155 in combination with oral ribociclib. A separate dose escalation was conducted for Japanese patients for the TNO155 plus ribociclib combination, given previous findings indicating that the maximum tolerated dose (MTD) of the combination of ribociclib with letrozole was lower in Japanese patients than in patients in the rest of the world (ROW).

It was planned to initiate the dose expansion part for the two combination treatments once the MTD or recommended dose (RD) had been declared. Following the study enrollment halt during the dose escalation part, the dose expansion part of the study was not started.

Centers

10 centers in 9 countries/regions: Belgium(1), Singapore(1), Australia(1), Japan(1), Spain(2), Germany(1), China(1), Hong Kong(1), United States(1)

Objectives:

The primary objective of the trial was to characterize the safety and tolerability of TNO155 in combination with spartalizumab and of TNO155 in combination with ribociclib, and to identify the MTD and/or recommended regimen (dose and schedule) for each combination.

The secondary objectives were:

- To characterize the pharmacokinetic (PK) profile of TNO155, spartalizumab, and ribociclib, when administered as a combination of TNO155 plus spartalizumab or of TNO155 plus ribociclib
- To evaluate the preliminary anti-tumor activity of TNO155 in combination with spartalizumab and of TNO155 in combination with ribociclib

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

The terms “investigational drug” and “study drug” were referred to TNO155, spartalizumab (PDR001), and ribociclib (LEE011).

The term “study treatment” referred to the following combination treatments:

- TNO155 in combination with spartalizumab
- TNO155 in combination with ribociclib

TNO155 in combination with spartalizumab

TNO155 was administered orally as a capsule on a 2 weeks on/1 week off schedule at dose levels ranging from 20 mg to 60 mg once a day (QD) and from 5 mg to 60 mg twice a day (BID).

Spartalizumab 300 mg was administered intravenously as a 30 minutes infusion once every 3 weeks.

TNO155 in combination with ribociclib

TNO155 was administered orally as a capsule on a 2 weeks on/1 week off schedule at dose levels ranging from 20 mg to 60 mg QD, and on a 3 weeks on/1 week off schedule at 40 mg QD and at dose levels ranging from 10 mg to 40 mg BID.

Ribociclib was administered orally as a capsule or tablet on a 2 weeks on/1 week off schedule at 200 mg QD, on a 3 weeks on/1 week off schedule at 150 mg or 200 mg QD, and on a continuous schedule at 200 mg QD.

The study treatment was administered until the patient experienced unacceptable toxicity, progressive disease, and/or had discontinued the treatment at the discretion of the Investigator or the patient, or due to withdrawal of consent.

Statistical Methods

Data for demographic and baseline characteristics, and efficacy, safety, pharmacokinetic and pharmacodynamics measurements was summarized using descriptive statistics. All analyses were performed by treatment group for each drug combination separately. PK profiles for the TNO155 plus ribociclib combination were presented separately for ROW and Japanese patients.

Analyses of dose-limiting toxicities (DLTs) were based on the Dose-Determining Set (DDS). The DDS includes all patients in the Full Analysis Set (all patients who received at least one dose of any study treatments) in dose escalation part who met the minimum exposure criteria and had sufficient safety evaluations or experienced a DLT during the DLT-evaluation period (Cycle 1, i.e. the first 21 or 28 days of dosing as applicable).

The safety analyses were conducted on the safety set (all patients who received at least one dose of any study treatments), which included all DLTs and all adverse events (AEs).

The efficacy endpoints were used to assess the preliminary anti-tumor activity of each combination treatment (i.e. TNO155 with spartalizumab and TNO155 with ribociclib). The endpoints included Overall Response Rate (ORR), Disease Control Rate (DCR), Duration of Response (DOR), Progression Free Survival (PFS), and Overall survival (OS). These were assessed per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1 for both study treatments and immune-related RECIST (iRECIST) for TNO155 with spartalizumab combination.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

1. Signed informed consent must be obtained prior to participation in the study.
2. Age ≥ 18 years.
   For Japan only: written consent is necessary both from the patient and his/her legal representative if he/she is under the age of 20 years.
3. ECOG (Eastern Cooperative Oncology Group) performance status ≤ 1.
4. Dose escalation part: Patients with advanced solid tumors, with evaluable disease as determined by RECIST version 1.1, and fit into one of the following groups:
   a. For TNO155 plus spartalizumab combination:
      i. Advanced EGFR WT, ALK WT NSCLC, after progression on or intolerance to platinum-containing combination chemotherapy and after progression on anti-PD-1 or anti-PD-L1 therapy.
      ii. Advanced HNSCC or esophageal SCC, after progression on or intolerance to platinum-containing combination chemotherapy.
      iii. Advanced CRC, after progression on or intolerance to all standard-of-care (SOC) therapy per local guidelines.

b. For TNO155 plus ribociclib combination:
Advanced solid malignancies with the exception of CRC or GIST, after progression on or intolerance to all SOC therapy per local guidelines. The exclusion of CRC applies only as of Protocol Amendment 4.

5. Dose expansion part: Patients with advanced solid tumors, with at least one measurable lesion as determined by RECIST version 1.1, who fit into one of the following groups:

c. For TNO155 plus spartalizumab combination:

i. Advanced EGFR WT, ALK WT, KRAS G12C NSCLC after progression on or intolerance to platinum-containing combination chemotherapy and after progression on anti-PD-1 or anti-PD-L1 therapy.

ii. Advanced EGFR WT, ALK WT, KRAS WT NSCLC, after progression on or intolerance to platinum-containing combination chemotherapy and after progression on anti-PD-1 or anti-PD-L1 therapy.

iii. Advanced HNSCC, after progression on or intolerance to, platinum-containing combination chemotherapy.

d. For TNO155 plus ribociclib combination:

i. Advanced EGFR WT, ALK WT, KRAS WT NSCLC, after progression on or intolerance to platinum-containing chemotherapy and anti-PD-1 or anti-PD-L1 therapy

ii. Advanced HNSCC, after progression on or intolerance to all SOC per local guidelines

6. Patients with NSCLC whose tumors harbor genomic aberrations for which SOC targeted therapies exist and are locally approved and available must have had progression on or after, or intolerance to, the SOC targeted therapy/therapies as indicated

7. Patients must have a site of disease amenable to biopsy

Key Exclusion Criteria:

1. Prior treatment with a MAPK pathway inhibitor
2. Clinically significant cardiac disease or risk factors
3. Use of any agent known to prolong the QT interval unless it can be permanently discontinued for the duration of study
4. History or current evidence of retinal vein occlusion (RVO) or current risk factors for RVO
5. Inflammatory bowel disease (e.g., ulcerative colitis, Crohn's disease) or impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of study drugs
6. Symptomatic CNS metastases which are neurologically unstable
7. Insufficient bone marrow function at screening:
    a. Absolute Neutrophil Count (ANC) < 1.5 x 109/L.
    b. Hemoglobin < 9.0 g/dL.
    c. Platelets < 75 x 109/L for TNO155 plus spartalizumab combination; < 100 x 109/L for TNO155 plus ribociclib combination.
8. Insufficient hepatic or renal function at screening:
    a. Serum total bilirubin > upper limit of normal (ULN) or, for TNO155 plus spartalizumab combination only, if liver metastases are present at baseline, serum total bilirubin > 1.5 x ULN. An exception for either combination is for patients with Gilbert's syndrome, who are excluded if total bilirubin > 3.0 x ULN or direct bilirubin > 1.5 x ULN
    b. Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 x ULN for TNO155 plus spartalizumab combination or > 2.5 x ULN for TNO155 plus ribociclib combination, or > 5 x ULN for either combination if liver metastases are present.

c. Creatinine clearance < 60 mL/min (calculated using Cockcroft-Gault equation).

9. Pregnant or breast-feeding (lactating) women.

Additional exclusion criteria for the TNO155 plus spartalizumab combination

10. History of severe hypersensitivity reactions to other mAbs.
11. Active, known or suspected autoimmune disease.
12. History of or current interstitial lung disease or pneumonitis grade ≥ 2.
13. Human Immunodeficiency Virus (HIV) infection, unless the patient is on antiviral therapy and has undetectable viral load.
14. Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection.
15. Systemic chronic steroid therapy
16. Patients who discontinued prior anti-PD-1 therapy due to an anti-PD-1-related toxicity.

Additional exclusion criteria for the TNO155 plus ribociclib combination

17. Systolic Blood Pressure (SBP) < 90 mmHg.
18. International Normalized Ratio (INR) > 1.5 (unless the patient is receiving anticoagulants and the INR is within the therapeutic range of intended use for that anticoagulant within seven days prior to the first dose of study drug).
19. History of HIV infection (testing not mandatory)
20. Currently receiving any of the following substances and cannot be discontinued seven days prior to Cycle 1 Day 1:
    - Concomitant medications or herbal supplements, that are strong inducers or inhibitors of CYP3A4/5,
    - Medications that have a narrow therapeutic window and are predominantly metabolized through CYP3A4/5.

21. Previous treatment with a CDK4/6 inhibitor.

22. Patient is currently receiving or has received systemic corticosteroids ≤ 2 weeks prior to starting study drug, or who have not fully recovered from side effects of such treatment.
    Note: The following uses of corticosteroids are permitted: single doses, topical applications (e.g., for rash), inhaled sprays (e.g., for obstructive airways diseases), eye drops or local injections (e.g., intra-articular).

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Participant Flow Table

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Started	5	19	6	5	5	6	7	3	1
Japan patients	0	0	0	0	0	0	0	0	0
Completed	0	0	0	0	0	0	0	0	0
Not Completed*	5	19	6	5	5	6	7	3	1
Progressive Disease	3	14	6	5	3	6	4	2	1
Adverse Event	0	3	0	0	0	0	1	1	0
Death	0	2	0	0	0	0	2	0	0
Patient Decision	1	0	0	0	2	0	0	0	0
Physician Decision	1	0	0	0	0	0	0	0	0

*Discontinued treatment

TNO155 + ribociclib, and Total

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	TNO155 40mg QD 2/1 + ribo 200mg QD cont	TNO155 60mg QD 2/1 + ribo 200mg QD cont	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1	TNO155 40mg QD 3/1 + ribo 200mg QD 3/1	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg QD 2/1 + ribo 200mg QD 2/1	TNO155 40mg QD 2/1 + ribo 200mg QD 2/1	Total
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	
Started	5	8	5	4	8	1	5	4	9	1	6	9	122
Japan patients	2	3	0	0	3	1	0	4	0	0	6	0	19
Completed	0	0	0	0	0	0	0	0	0	0	0	0	0
Not Completed*	5	8	5	4	8	1	5	4	9	1	6	9	122
Progressive Disease	4	7	3	4	7	1	5	3	8	0	6	8	100

Adverse Event	1	1	1	0	0	0	0	1	1	1	0	0	11
Death	0	0	0	0	1	0	0	0	0	0	0	0	5
Patient Decision	0	0	1	0	0	0	0	0	0	0	0	1	5
Physician Decision	0	0	0	0	0	0	0	0	0	0	0	0	1

*Discontinued treatment

Baseline Characteristics

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants	5	19	6	5	5	6	7	3	1

[units: participants]									
Baseline Analysis Population Description									
Age Continuous (units: years) Analysis Population Type: Participants Mean ± Standard Deviation									
	51.0±7.07	57.9±10.76	60.0±12.46	55.8±5.07	55.0±15.28	60.0±9.53	53.3±16.73	52.0±13.23	66.0
Age, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
18 - < 65 years	5	12	4	5	3	4	6	3	0
65 - <85 years	0	7	2	0	2	2	1	0	1
>= 85 years	0	0	0	0	0	0	0	0	0
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
Female	3	4	3	2	2	3	4	1	0
Male	2	15	3	3	3	3	3	2	1
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)									
Asian	2	3	1	2	2	2	3	1	0
White	3	16	5	3	3	4	4	2	1
Unknown	0	0	0	0	0	0	0	0	0
Study Specific Characteristic Diagnosis of Disease									

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

Ampula of Vater Cancer	0	0	0	0	0	0	0	0	0
Breast Cancer	0	0	0	0	0	0	0	0	0
Colorectal Cancer	4	5	4	5	2	6	5	2	1
Esophageal Cancer	0	0	1	0	0	0	1	0	0
Gallbladder Cancer	0	0	0	0	0	0	0	0	0
Gastrointestinal Stromal Tumor	0	0	0	0	0	0	0	0	0
Head And Neck Cancer	1	6	0	0	0	0	0	1	0
Larynx Carcinoma	0	1	0	0	0	0	0	0	0
Liposarcoma	0	0	0	0	0	0	0	0	0
Malignant Melanoma	0	0	0	0	0	0	0	0	0
Nasopharyngeal Cancer	0	0	0	0	0	0	0	0	0
Non-Small Cell Lung Cancer	0	7	1	0	3	0	1	0	0
Pancreatic Carcinoma	0	0	0	0	0	0	0	0	0
Soft Tissue Sarcoma	0	0	0	0	0	0	0	0	0
Thymus Lymphoepithelioma	0	0	0	0	0	0	0	0	0

Thyroid Cancer	0	0	0	0	0	0	0	0	0				

TNO155 + ribociclib, and Total

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**	**Total**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	
Number of Participants [units: participants]	5	8	5	4	8	1	5	4	9	1	6	9	122
Baseline Analysis Population Description													
Age Continuous (units: years)													

Analysis Population Type: Participants
Mean ± Standard Deviation

	59.8±10.43	48.4±10.95	47.8±6.69	53.3±12.55	59.0±8.80	57.0	63.6±12.32	47.3±20.47	61.7±12.08	70.0	61.8±12.22	55.4±9.46	57±12
Age, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													
18 - < 65 years	3	7	5	4	6	1	3	3	4	0	3	8	89
65 - <85 years	2	1	0	0	2	0	2	1	5	1	3	1	33
>= 85 years	0	0	0	0	0	0	0	0	0	0	0	0	0
Sex: Female, Male (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													
Female	0	5	3	3	5	0	3	2	3	0	3	4	53
Male	5	3	2	1	3	1	2	2	6	1	3	5	69
Race/Ethnicity, Customized (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													
Asian	2	4	1	2	4	1	0	4	3	1	6	5	49
White	3	4	3	2	4	0	5	0	6	0	0	4	72
Unknown	0	0	1	0	0	0	0	0	0	0	0	0	1
Study Specific Characteristic Diagnosis of Disease (units: participants) Analysis Population Type: Participants Count of Participants (Not Applicable)													
Ampula of Vater Cancer	0	0	0	0	0	0	0	0	0	0	1	0	1

Breast Cancer	0	0	0	0	0	0	0	0	0	0	1	1	2
Colorectal Cancer	4	7	3	2	6	0	4	1	7	0	0	0	68
Esophageal Cancer	0	0	0	0	0	1	1	0	1	1	0	0	6
Gallbladder Cancer	0	0	0	0	0	0	0	0	0	0	1	0	1
Gastrointestinal Stromal Tumor	1	0	0	1	0	0	0	2	0	0	0	1	5
Head And Neck Cancer	0	0	0	0	1	0	0	1	0	0	0	1	11
Larynx Carcinoma	0	0	0	0	0	0	0	0	0	0	0	0	1
Liposarcoma	0	0	0	0	0	0	0	0	0	0	0	1	1
Malignant Melanoma	0	0	0	0	0	0	0	0	0	0	1	0	1
Nasopharyngeal Cancer	0	0	0	0	0	0	0	0	0	0	0	1	1
Non-Small Cell Lung Cancer	0	1	2	1	1	0	0	0	1	0	0	2	20
Pancreatic Carcinoma	0	0	0	0	0	0	0	0	0	0	1	0	1
Soft Tissue Sarcoma	0	0	0	0	0	0	0	0	0	0	0	1	1
Thymus Lymphoepithelioma	0	0	0	0	0	0	0	0	0	0	0	1	1
Thyroid Cancer	0	0	0	0	0	0	0	0	0	0	1	0	1

Primary Outcome Result(s)

Number of participants with Dose-Limiting Toxicities (DLTs) – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients)

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 evaluation period is the first cycle of treatment (either 21 or 28 days from the start of treatment, depending on the dosing schedule). Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher.
Time Frame	First cycle of treatment (either 21 or 28 days from the start of treatment, depending on the dosing schedule)
Analysis Population Description	Dose-Determining Set (DDS) including all patients who received at least one dose of any study treatment in the dose escalation part who met the minimum exposure criteria and had sufficient safety evaluations or experienced a DLT during the DLT-evaluation period (Cycle 1). For TNO155 plus ribociclib, only patients from rest of world (ROW) excluding Japan are considered for this endpoint.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed	4	15	6	3	5	4	4	2	0

[units: participants]									
Number of participants with Dose-Limiting Toxicities (DLTs) – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (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)**
	2 (50%)	1 (6.67%)	0 (%)	0 (%)	1 (20%)	0 (%)	1 (25%)	2 (100%)	(NaN%)

TNO155 + ribociclib (ROW patients)

	TNO155 20mg QD 2/1 + ribo 200mg QD cont_ROW	**TNO155 40mg QD 2/1 + ribo 200mg QD cont_ROW**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont_ROW**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1_ROW**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1_ROW**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1_ROW**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off
Number of Participants	3	3	5	3	2	4	7	1	7

Analyzed [units: participants]									
Number of participants with Dose-Limiting Toxicities (DLTs) – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (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)**
	0 (%)	1 (33.33%)	2 (40%)	1 (33.33%)	0 (%)	0 (%)	3 (42.86%)	1 (100%)	1 (14.29%)

Number of participants with Dose-Limiting Toxicities (DLTs) – TNO155 plus ribociclib (Japan patients)

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 evaluation period is the first cycle of treatment (either 21 or 28 days from the start of treatment, depending on the dosing schedule). Other clinically significant toxicities may be considered to be DLTs, even if not CTCAE grade 3 or higher.
Time Frame	First cycle of treatment (either 21 or 28 days from the start of treatment, depending on the dosing schedule)
Analysis Population Description	Dose-Determining Set (DDS) including all patients who received at least one dose of any study treatment in the dose escalation part who met the minimum exposure criteria and had sufficient safety evaluations or experienced a DLT during the DLT-evaluation period (Cycle 1). Only patients from Japan treated with TNO155 plus ribociclib are considered for this endpoint.

	TNO155 20mg QD 2/1 + ribo	**TNO155 40mg QD 2/1 + ribo**	**TNO155 40mg QD 3/1 + ribo**	**TNO155 10mg BID 3/1 + ribo**	**TNO155 20mg BID 3/1 + ribo**	**TNO155 20mg QD 2/1 + ribo**

	200mg QD cont_JP	200mg QD cont_JP	200mg QD 3/1_JP	200mg QD 3/1_JP	200mg QD 3/1_JP	200mg QD 2/1_JP
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off
Number of Participants Analyzed [units: participants]	2	2	3	1	3	4
Number of participants with Dose-Limiting Toxicities (DLTs) – TNO155 plus ribociclib (Japan patients) (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)**
	0 (%)	2 (100%)	2 (66.67%)	0 (%)	1 (33.33%)	0 (%)

Number of participants with AEs and SAEs during the on-treatment period – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients)

Description	Number of participants with AEs (any adverse events regardless of seriousness) and serious adverse events (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 any study treatment up to 30 days after the date of the last actual administration of any study drug.
Time Frame	Up to approximately 1.8 years (TNO155+spartalizumab) and 1.5 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of any study treatment. For TNO155 plus ribociclib, only patients from rest of world (ROW) excluding Japan are considered for this endpoint.

TNO155 + spartalizumab

	TNO155 20mg QD	TNO155 60mg QD	TNO155 5mg BID 2/1	TNO155 10mg BID	TNO155 20mg BID	TNO155 30mg BID	TNO155 40mg BID	TNO155 50mg BID	TNO155 60mg BID

	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	+ sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1
Number of participants with AEs and SAEs during the on-treatment period – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (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)**
AEs	5 (100%)	19 (100%)	6 (100%)	5 (100%)	5 (100%)	6 (100%)	7 (100%)	3 (100%)	1 (100%)
Treatment-related AEs	5 (100%)	18 (94.74%)	5 (83.33%)	5 (100%)	5 (100%)	6 (100%)	6 (85.71%)	3 (100%)	1 (100%)
SAEs	2 (40%)	12 (63.16%)	3 (50%)	3 (60%)	4 (80%)	4 (66.67%)	6 (85.71%)	2 (66.67%)	1 (100%)

Treatment-related SAEs	0 (%)	3 (15.79%)	2 (33.33%)	0 (%)	2 (40%)	2 (33.33%)	1 (14.29%)	1 (33.33%)	0 (%)

TNO155 + ribociclib (ROW patients)

	TNO155 20mg QD 2/1 + ribo 200mg QD cont_ROW	**TNO155 40mg QD 2/1 + ribo 200mg QD cont_ROW**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont_ROW**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1_ROW**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1_ROW**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1_ROW**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off
Number of Participants Analyzed [units: participants]	3	5	5	4	5	5	9	1	9
Number of participants with AEs and SAEs during the on-treatment period – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients)	**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)**

(units: participants)									
AEs	3 (100%)	5 (100%)	5 (100%)	4 (100%)	5 (100%)	5 (100%)	9 (100%)	1 (100%)	9 (100%)
Treatment-related AEs	3 (100%)	5 (100%)	5 (100%)	3 (75%)	5 (100%)	4 (80%)	8 (88.89%)	1 (100%)	7 (77.78%)
SAEs	2 (66.67%)	3 (60%)	2 (40%)	3 (75%)	1 (20%)	2 (40%)	4 (44.44%)	1 (100%)	5 (55.56%)
Treatment-related SAEs	0 (%)	1 (20%)	2 (40%)	1 (25%)	0 (%)	0 (%)	0 (%)	1 (100%)	0 (%)

Number of participants with AEs and SAEs during the on-treatment period – TNO155 plus ribociclib (Japan patients)

Description	Number of participants with AEs (any adverse events regardless of seriousness) and serious adverse events (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 any study treatment up to 30 days after the date of the last actual administration of any study drug.
Time Frame	Up to approximately 1.5 years
Analysis Population Description	All patients who received at least one dose of any study treatment. Only patients from Japan treated with TNO155 plus ribociclib are considered for this endpoint.

	TNO155 20mg QD 2/1 + ribo 200mg QD cont_JP	**TNO155 40mg QD 2/1 + ribo 200mg QD cont_JP**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1_JP**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off

Number of Participants Analyzed [units: participants]	2	3	3	1	4	6
Number of participants with AEs and SAEs during the on-treatment period – TNO155 plus ribociclib (Japan patients) (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)**
AEs	2 (100%)	3 (100%)	3 (100%)	1 (100%)	4 (100%)	6 (100%)
Treatment-related AEs	2 (100%)	3 (100%)	3 (100%)	1 (100%)	4 (100%)	6 (100%)
SAEs	0 (%)	1 (33.33%)	1 (33.33%)	1 (100%)	0 (%)	2 (33.33%)
Treatment-related SAEs	0 (%)	0 (%)	1 (33.33%)	0 (%)	0 (%)	0 (%)

Number of participants with dose reductions and dose interruptions of TNO155

Description	Number of participants with at least one dose reduction and at least one dose interruption of TNO155. Dose adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule.
Time Frame	Up to approximately 1.7 years (TNO155+spartalizumab) and 1.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of TNO155

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off	TNO155 60 mg oral QD 2w on/1w off	TNO155 5 mg oral BID 2w on/1w off	TNO155 10 mg oral BID 2w on/1w off	TNO155 20 mg oral BID 2w on/1w off	TNO155 30 mg oral BID 2w on/1w off	TNO155 40 mg oral BID 2w on/1w off	TNO155 50 mg oral BID 2w on/1w off	TNO155 60 mg oral BID 2w on/1w off

	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1
Number of participants with dose reductions and dose interruptions of TNO155 (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)**
At least one dose reduction or interruption	5 (100%)	9 (47.37%)	4 (66.67%)	4 (80%)	4 (80%)	6 (100%)	6 (85.71%)	1 (33.33%)	1 (100%)
At least one dose reduction	1 (20%)	3 (15.79%)	1 (16.67%)	0 (%)	2 (40%)	0 (%)	2 (28.57%)	1 (33.33%)	0 (%)
At least one dose interruption	5 (100%)	9 (47.37%)	4 (66.67%)	4 (80%)	3 (60%)	6 (100%)	5 (71.43%)	1 (33.33%)	1 (100%)

TNO155 + ribociclib

TNO155 20mg QD 2/1 + ribo	**TNO155 40mg QD 2/1 + ribo**	**TNO155 60mg QD 2/1 + ribo**	**TNO155 40mg QD 3/1 + ribo**	**TNO155 40mg QD 3/1 + ribo**	**TNO155 10mg BID 3/1 + ribo**	**TNO155 20mg BID 3/1 + ribo**	**TNO155 20mg BID 3/1 + ribo**	**TNO155 30mg BID 3/1 + ribo**	**TNO155 40mg BID 3/1 + ribo**	**TNO155 20mg QD 2/1 + ribo**	**TNO155 40mg QD 2/1 + ribo**

	200mg QD cont	200mg QD cont	200mg QD cont	150mg QD 3/1	200mg QD 3/1	200mg QD 3/1	150mg QD 3/1	200mg QD 3/1	200mg QD 3/1	200mg QD 3/1	200mg QD 2/1	200mg QD 2/1
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off
Number of Participants Analyzed [units: participants]	5	8	5	4	8	1	5	4	9	1	6	9
Number of participants with dose reductions and dose interruptions of TNO155 (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)**
At least one dose reduction or	3 (60%)	6 (75%)	3 (60%)	2 (50%)	5 (62.5%)	1 (100%)	1 (20%)	3 (75%)	8 (88.89%)	1 (100%)	4 (66.67%)	8 (88.89%)

interruption												
At least one dose reduction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	1 (11.11%)	0 (%)	0 (%)	2 (22.22%)
At least one dose interruption	3 (60%)	6 (75%)	3 (60%)	2 (50%)	5 (62.5%)	1 (100%)	1 (20%)	3 (75%)	7 (77.78%)	1 (100%)	4 (66.67%)	8 (88.89%)

Number of participants with dose reductions and dose interruptions of spartalizumab

Description	Number of participants with at least one dose reduction and at least one dose interruption of spartalizumab. Dose interruptions were permitted for patients who did not tolerate the protocol-specified dosing schedule. Dose reductions were not permitted for spartalizumab.
Time Frame	Up to approximately 1.7 years
Analysis Population Description	All patients who received at least one dose of spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants	5	19	6	5	5	6	7	3	1

Analyzed [units: participants]									
Number of participants with dose reductions and dose interruptions of spartalizumab (units: participants)	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**	**Count of Participants (Percentage)**
At least one dose reduction or interruption	3 (60%)	5 (26.32%)	3 (50%)	1 (20%)	1 (20%)	3 (50%)	1 (14.29%)	0 (%)	0 (%)
At least one dose reduction	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)	0 (%)
At least one dose interruption	3 (60%)	5 (26.32%)	3 (50%)	1 (20%)	1 (20%)	3 (50%)	1 (14.29%)	0 (%)	0 (%)

Number of participants with dose reductions and dose interruptions of ribociclib

Description	Number of participants with at least one dose reduction and at least one dose interruption of ribociclib. Dose adjustments were permitted for patients who did not tolerate the protocol-specified dosing schedule.
Time Frame	Up to approximately 1.4 years
Analysis Population Description	All patients who received at least one dose of ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	TNO155 40mg QD 2/1 + ribo 200mg QD cont	TNO155 60mg QD 2/1 + ribo 200mg QD cont	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1	TNO155 40mg QD 3/1 + ribo 200mg QD 3/1	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg QD 2/1 + ribo 200mg QD 2/1	TNO155 40mg QD 2/1 + ribo 200mg QD 2/1
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off
Number of Participants Analyzed [units: participants]	5	8	5	4	8	1	5	4	9	1	6	9
Number of participants with dose reductions and dose interruptions of ribociclib (units:	**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)**

participants)												
At least one dose reduction or interruption	3 (60%)	6 (75%)	3 (60%)	2 (50%)	5 (62.5%)	1 (100%)	1 (20%)	3 (75%)	6 (66.67%)	0 (%)	4 (66.67%)	8 (88.89%)
At least one dose reduction	0 (%)	0 (%)	0 (%)	1 (25%)	2 (25%)	0 (%)	0 (%)	1 (25%)	2 (22.22%)	0 (%)	0 (%)	1 (11.11%)
At least one dose interruption	3 (60%)	6 (75%)	3 (60%)	2 (50%)	5 (62.5%)	1 (100%)	1 (20%)	3 (75%)	5 (55.56%)	0 (%)	4 (66.67%)	8 (88.89%)

Dose intensity of TNO155

Description	Dose intensity of TNO155 was calculated as cumulative actual dose in milligrams divided by duration of exposure in days.
Time Frame	Up to approximately 1.7 years (TNO155+spartalizumab) and 1.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of TNO155

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination	TNO155 60 mg oral QD 2w on/1w off in combination	TNO155 5 mg oral BID 2w on/1w off in combination	TNO155 10 mg oral BID 2w on/1w off in combination	TNO155 20 mg oral BID 2w on/1w off in combination	TNO155 30 mg oral BID 2w on/1w off in combination	TNO155 40 mg oral BID 2w on/1w off in combination	TNO155 50 mg oral BID 2w on/1w off in combination	TNO155 60 mg oral BID 2w on/1w off in combination

	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W	with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1
Dose intensity of TNO155 (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)**
	11.5 (3 to 20)	53.6 (12 to 60)	8.7 (7 to 16)	15.6 (9 to 20)	36.2 (20 to 40)	38.7 (11 to 52)	42.7 (29 to 76)	59.2 (27 to 97)	60.0 (60 to 60)

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD

	continuous	continuous	continuous	3w on/1w off	3w on/1w off	3w on/1w off	3w on/1w off	3w on/1w off	3w on/1w off	3w on/1w off	2w on/1w off	2w on/1w off
Number of Participants Analyzed [units: participants]	5	8	5	4	8	1	5	4	9	1	6	9
Dose intensity of TNO155 (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)**
	20.0 (14 to 20)	40.0 (36 to 40)	60.0 (50 to 60)	40.0 (21 to 40)	40.0 (20 to 40)	20.0 (20 to 20)	40.0 (27 to 40)	36.6 (29 to 40)	58.6 (30 to 60)	31.3 (31.3 to 31.3)	18.8 (9 to 20)	30.5 (19 to 40)

Dose intensity of spartalizumab

Description	Dose intensity of spartalizumab was calculated as cumulative actual dose in milligrams divided by duration of exposure in days.
Time Frame	Up to approximately 1.7 years
Analysis Population Description	All patients who received at least one dose of spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off	TNO155 60 mg oral QD 2w on/1w off	TNO155 5 mg oral BID 2w on/1w off	TNO155 10 mg oral BID 2w on/1w off	TNO155 20 mg oral BID 2w on/1w off	TNO155 30 mg oral BID 2w on/1w off	TNO155 40 mg oral BID 2w on/1w off	TNO155 50 mg oral BID 2w on/1w off	TNO155 60 mg oral BID 2w on/1w off

	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1
Dose intensity of spartalizumab (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)**
	12.5 (11 to 18)	13.8 (6 to 38)	13.4 (11 to 17)	14.3 (12 to 18)	14.1 (9 to 16)	12.9 (11 to 22)	15.8 (9 to 23)	20.0 (16 to 43)	21.4 (21.4 to 21.4)

Dose intensity of ribociclib

Description	Dose intensity of ribociclib was calculated as cumulative actual dose in milligrams divided by duration of exposure in days.
Time Frame	Up to approximately 1.4 years
Analysis Population Description	All patients who received at least one dose of ribociclib

TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**

Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off
Number of Participants Analyzed [units: participants]	5	8	5	4	8	1	5	4	9	1	6	9
Dose intensity of ribociclib (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)**
	177.8 (78 to 200)	200.0 (175 to 200)	200.0 (178 to 200)	150.0 (39 to 150)	200.0 (84 to 200)	200.0 (200 to 200)	150.0 (100 to 153)	174.3 (138 to 200)	200.0 (108 to 200)	200.0 (200 to 200)	188.1 (87 to 200)	159.6 (100 to 200)

NOVARTIS

Secondary Outcome Result(s)

Overall Response Rate (ORR) per RECIST v1.1

Description	ORR is the percentage of patients with a confirmed 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 1.7 years (TNO155+spartalizumab) and 1.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of study treatment.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W	TNO155 + sparta patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units:	5	19	6	5	5	6	7	3	1	57

participants]										
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)**
	0 (0.0 to 45.1)	5.3 (0.3 to 22.6)	0 (0.0 to 39.3)	0 (0.0 to 45.1)	0 (0.0 to 45.1)	0 (0.0 to 39.3)	0 (0.0 to 34.8)	0 (0.0 to 63.2)	0 (0.0 to 95.0)	1.8 (0.1 to 8.1)

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 + ribo patients**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	All patients who received TNO155 in combination with ribociclib

Number of Participants Analyzed [units: participants]	5	8	5	1	5	4	9	4	8	1	6	9	65
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 45.1)	0 (0.0 to 31.2)	0 (0.0 to 45.1)	0 (0.0 to 95.0)	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 31.2)	0 (0.0 to 95.0)	0 (0.0 to 39.3)	0 (0.0 to 28.3)	0 (0.0 to 4.5)

Disease Control Rate (DCR) per RECIST v1.1

Description	DCR is the percentage of patients with a confirmed 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 1.7 years (TNO155+spartalizumab) and 1.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of study treatment.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W	TNO155 + sparta patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1	57
Disease Control Rate (DCR) per RECIST v1.1 (units: percentage of participants)	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**	**Number (90% Confidence Interval)**
	40.0 (7.6 to 81.1)	31.6 (14.7 to 53.0)	50.0 (15.3 to 84.7)	20.0 (1.0 to 65.7)	40.0 (7.6 to 81.1)	16.7 (0.9 to 58.2)	0 (0.0 to 34.8)	0 (0.0 to 63.2)	0 (0.0 to 95.0)	26.3 (17.0 to 37.6)

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 + ribo patients**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	All patients who received TNO155 in combination with ribociclib
Number of Participants Analyzed [units: participants]	5	8	5	1	5	4	9	4	8	1	6	9	65
Disease Control Rate (DCR) per RECIST v1.1 (units: percentage of	**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)**

participants)	0 (0.0 to 45.1)	12.5 (0.6 to 47.1)	0 (0.0 to 45.1)	0 (0.0 to 95.0)	0 (0.0 to 45.1)	50.0 (9.8 to 90.2)	11.1 (0.6 to 42.9)	0 (0.0 to 52.7)	12.5 (0.6 to 47.1)	0 (0.0 to 95.0)	0 (0.0 to 39.3)	44.4 (16.9 to 74.9)	13.8 (7.4 to 22.9)

Overall Response Rate (iORR) per iRECIST – TNO155 plus spartalizumab

Description	iORR is the percentage of patients with first confirmed 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 1.7 years
Analysis Population Description	All patients who received at least one dose of TNO155 in combination with spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**	**TNO155 + sparta patients**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed	5	19	6	5	5	6	7	3	1	57

[units: participants]										
Overall Response Rate (iORR) per iRECIST – TNO155 plus spartalizumab (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)**
	0 (0.0 to 45.1)	5.3 (0.3 to 22.6)	0 (0.0 to 39.3)	0 (0.0 to 45.1)	0 (0.0 to 45.1)	0 (0.0 to 39.3)	0 (0.0 to 34.8)	0 (0.0 to 63.2)	0 (0.0 to 95.0)	1.8 (0.1 to 8.1)

Disease Control Rate (iDCR) per iRECIST – TNO155 plus spartalizumab

Description	iDCR is the percentage of patients with first confirmed 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 1.7 years
Analysis Population Description	All patients who received at least one dose of TNO155 in combination with spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**	**TNO155 + sparta patients**
Arm/Group Description	TNO155 20 mg oral QD	TNO155 60 mg oral QD	TNO155 5 mg oral	TNO155 10 mg oral	TNO155 20 mg oral	TNO155 30 mg oral	TNO155 40 mg oral	TNO155 50 mg oral	TNO155 60 mg oral	All patients who

	2w on/1w off in combination with spartalizumab 300 mg IV Q3W	2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1	57
Disease Control Rate (iDCR) per iRECIST – TNO155 plus spartalizumab (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)**
	40.0 (7.6 to 81.1)	26.3 (11.0 to 47.6)	50.0 (15.3 to 84.7)	20.0 (1.0 to 65.7)	40.0 (7.6 to 81.1)	16.7 (0.9 to 58.2)	0 (0.0 to 34.8)	0 (0.0 to 63.2)	0 (0.0 to 95.0)	24.6 (15.5 to 35.7)

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

Description	PFS per RECIST v1.1 is defined as the time from the date of start of treatment to the date of the first documented progression as per local review and according to RECIST v1.1 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 2.1 years (TNO155+spartalizumab) and 1.5 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of study treatment.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W	TNO155 + sparta patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1	57
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)**
	3.58 (1.54 to NA)[1]	1.94 (1.74 to 3.52)	4.12 (1.64 to 8.34)	1.84 (0.56 to NA)[1]	1.92 (1.81 to NA)[1]	1.25 (0.39 to NA)[1]	1.38 (0.49 to 2.04)	1.84 (NA to NA)[1]	0.85 (NA to NA)[1]	1.84 (1.74 to 2.00)

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

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	TNO155 40mg QD 2/1 + ribo 200mg QD cont	TNO155 60mg QD 2/1 + ribo 200mg QD cont	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1	TNO155 40mg QD 3/1 + ribo 200mg QD 3/1	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg QD 2/1 + ribo 200mg QD 2/1	TNO155 40mg QD 2/1 + ribo 200mg QD 2/1	TNO155 + ribo patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	All patients who received TNO155 in combination with ribociclib
Number of Participants Analyzed [units: participants]	5	8	5	1	5	4	9	4	8	1	6	9	65
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)**

1.86 (1.61 to NA)[1]	1.03 (0.33 to 1.77)	1.76 (1.64 to NA)[1]	2.33 (NA to NA)[1]	1.71 (0.99 to NA)[1]	2.25 (0.82 to NA)[1]	1.68 (0.69 to 1.81)	1.84 (0.76 to NA)[1]	1.68 (0.85 to 2.17)	1.94 (NA to NA)[1]	1.76 (0.33 to NA)[1]	2.04 (1.02 to 9.72)	1.79 (1.64 to 1.87)

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

Progression-Free Survival (iPFS) per iRECIST – TNO155 plus spartalizumab

Description	iPFS per iRECIST is defined as the time from the date of start of treatment to the date of the first documented confirmed progression as per local review and according to iRECIST 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 2.1 years
Analysis Population Description	All patients who received at least one dose of TNO155 in combination with spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**	**TNO155 + sparta patients**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1	57

Progression-Free Survival (iPFS) per iRECIST – TNO155 plus spartalizumab (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)
	3.58 (1.54 to NA)[1]	1.84 (1.45 to 3.52)	4.12 (1.64 to NA)[1]	1.87 (0.56 to NA)[1]	1.92 (1.81 to NA)[1]	1.25 (0.39 to NA)[1]	1.38 (0.49 to 2.04)	1.84 (NA to NA)[1]	0.85 (NA to NA)[1]	1.84 (1.74 to 2.00)

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

Duration of Response (DOR) per RECIST v1.1

Description	DOR per RECIST v1.1 is defined as the time from the CR or PR to the date of progression or death due to study indication. DOR only applies to patients with a best overall response of CR or PR per RECIST v1.1. DOR was analyzed using the Kaplan-Meier method.
Time Frame	Up to approximately 1.7 years (TNO155+spartalizumab) and 1.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of study treatment and had a best overall response of CR or PR.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W	TNO155 + sparta patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combinatio	TNO155 60 mg oral QD 2w on/1w off in combinatio	TNO155 5 mg oral BID 2w on/1w off in combinatio	TNO155 10 mg oral BID 2w on/1w off in combinatio	TNO155 20 mg oral BID 2w on/1w off in combinatio	TNO155 30 mg oral BID 2w on/1w off in combinatio	TNO155 40 mg oral BID 2w on/1w off in combinatio	TNO155 50 mg oral BID 2w on/1w off in combinatio	TNO155 60 mg oral BID 2w on/1w off in combinatio	All patients who received TNO155 in combinatio

	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab 300 mg IV Q3W	n with spartalizumab ab
Number of Participants Analyzed [units: participants]	0	1	0	0	0	0	0	0	0	1
Duration of Response (DOR) 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)**
		14.88 (NA to NA)[1]								14.88 (NA to NA)[1]

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

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 + ribo patients**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combina	TNO155 40 mg oral QD 2w on/1w off in combina	TNO155 60 mg oral QD 2w on/1w off in combina	TNO155 10 mg oral BID 3w on/1w off in combina	TNO155 20 mg oral BID 3w on/1w off in combina	TNO155 20 mg oral BID 3w on/1w off in combina	TNO155 30 mg oral BID 3w on/1w off in combina	TNO155 40 mg oral QD 3w on/1w off in combina	TNO155 40 mg oral QD 3w on/1w off in combina	TNO155 40 mg oral BID 3w on/1w off in combina	TNO155 20 mg oral QD 2w on/1w off in combina	TNO155 40 mg oral QD 2w on/1w off in combina	All patients who received TNO155 in combina

	tion with ribocicli b 200 mg oral QD continuous	tion with ribocicli b 200 mg oral QD continuous	tion with ribocicli b 200 mg oral QD continuous	tion with ribocicli b 200 mg oral QD 3w on/1w off	tion with ribocicli b 150 mg oral QD 3w on/1w off	tion with ribocicli b 200 mg oral QD 3w on/1w off	tion with ribocicli b 200 mg oral QD 3w on/1w off	tion with ribocicli b 150 mg oral QD 3w on/1w off	tion with ribocicli b 200 mg oral QD 3w on/1w off	tion with ribocicli b 200 mg oral QD 3w on/1w off	tion with ribocicli b 200 mg oral QD 2w on/1w off	tion with ribocicli b 200 mg oral QD 2w on/1w off	tion with ribociclib
Number of Participants Analyzed [units: participants]	0	0	0	0	0	0	0	0	0	0	0	0	0
Duration of Response (DOR) 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] Not estimable due to insufficient number of participants with events.

Duration of Response (iDOR) per iRECIST – TNO155 plus spartalizumab

Description	iDOR per iRECIST is defined as the time from the iCR or iPR to the date of confirmed progression or death due to study indication. iDOR only applies to patients with a best overall response of iCR or iPR per iRECIST. DOR was analyzed using the Kaplan-Meier method.
Time Frame	Up to approximately 1.7 years
Analysis Population Description	All patients who received at least one dose of TNO155 in combination with spartalizumab. and had a best overall response of iCR or iPR.

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W	TNO155 + sparta patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units: participants]	0	1	0	0	0	0	0	0	0	1
Duration of Response (iDOR) per iRECIST – TNO155 plus spartalizumab (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)**
		12.94 (NA to NA)[1]								12.94 (NA to NA)[1]

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

Overall Survival (OS)

Description Overall survival is defined as the time from the start of treatment to the date of death due to any cause. OS was analyzed using the Kaplan-Meier method.

Time Frame	Up to approximately 3.7 years (TNO155+spartalizumab) and 2.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of study treatment.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**	**TNO155 + sparta patients**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	All patients who received TNO155 in combination with spartalizumab
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1	57
Overall Survival (OS) (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)**
	17.71 (1.54 to NA)[1]	11.30 (3.52 to 18.89)	13.98 (2.60 to 16.13)	5.52 (1.74 to NA)[1]	10.92 (8.64 to NA)[1]	5.19 (2.14 to NA)[1]	2.56 (0.49 to 6.37)	8.02 (4.14 to NA)[1]	4.57 (NA to NA)[1]	8.44 (5.52 to 13.32)

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

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	TNO155 40mg QD 2/1 + ribo 200mg QD cont	TNO155 60mg QD 2/1 + ribo 200mg QD cont	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1	TNO155 40mg QD 3/1 + ribo 200mg QD 3/1	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1	TNO155 20mg QD 2/1 + ribo 200mg QD 2/1	TNO155 40mg QD 2/1 + ribo 200mg QD 2/1	TNO155 + ribo patients
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD 2w on/1w off	All patients who received TNO155 in combination with ribociclib
Number of Participants Analyzed [units: participants]	5	8	5	1	5	4	9	4	8	1	6	9	65
Overall Survival (OS) (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)**

6.01 (5.78 to NA)[1]	6.77 (2.56 to 14.49)	12.39 (4.93 to NA)[1]	4.07 (NA to NA)[1]	8.64 (2.96 to NA)[1]	NA (5.52 to NA)[1]	5.36 (2.23 to 6.18)	12.06 (1.51 to NA)[1]	18.20 (2.17 to NA)[1]	1.94 (NA to NA)[1]	5.26 (3.94 to NA)[1]	NA (5.26 to NA)[1]	6.67 (5.95 to 9.43)

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

Maximum observed plasma concentration (Cmax) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients)

Description	Pharmacokinetic (PK) parameters were calculated based on TNO155 plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 (TNO155+ribociclib only), 5 (TNO155+spartalizumab only) and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received TNO155 in combination with spartalizumab or ribociclib and had an available value for the outcome measure. For TNO155 plus ribociclib, only patients from rest of world (ROW) excluding Japan are considered for this endpoint. PAS consisted of all patients who provided an evaluable PK profile.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed	4	12	6	3	4	4	2	0	0

[units: participants]									
Maximum observed plasma concentration (Cmax) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	141 (32.1%)	457 (39.2%)	65.3 (40.4%)	112 (28.1%)	199 (53.1%)	295 (38.7%)	742 (52.3%)		

TNO155 + ribociclib (ROW)

	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1_ROW	**TNO155 20mg QD 2/1 + ribo 200mg QD cont_ROW**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 40mg QD + ribo 200mg QD combined_ROW**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1_ROW**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1_ROW**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont_ROW**
Arm/Group Description	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous, 2w on/1w off and 3w on/1w off)	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous
Number of Participants Analyzed	4	3	5	13	3	0	3

[units: participants]							
Maximum observed plasma concentration (Cmax) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	203 (15.7%)	167 (3.3%)	369 (20.2%)	280 (65.3%)	349 (29.6%)		512 (28.2%)

Time to maximum observed plasma concentration (Tmax) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients)

Description	PK parameters were calculated based on TNO155 plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) observed concentration following a dose. Actual sampling times were considered for the calculation of PK parameters.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 (TNO155+ribociclib only), 5 (TNO155+spartalizumab only) and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received TNO155 in combination with spartalizumab or ribociclib and had an available value for the outcome measure. For TNO155 plus ribociclib, only patients from rest of world (ROW) excluding Japan are considered for this endpoint. PAS consisted of all patients who provided an evaluable PK profile.

TNO155 + spartalizumab

TNO155 20mg QD	**TNO155 60mg QD**	**TNO155 5mg BID 2/1**	**TNO155 10mg BID**	**TNO155 20mg BID**	**TNO155 30mg BID**	**TNO155 40mg BID**	**TNO155 50mg BID**	**TNO155 60mg BID**

	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	+ sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W	2/1 + sparta 300mg Q3W
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	4	12	6	3	4	4	2	0	0
Time to maximum observed plasma concentration (Tmax) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	4.68 (2.00 to 5.00)	2.00 (0.967 to 5.35)	1.96 (1.02 to 2.08)	2.12 (1.00 to 4.00)	2.10 (2.00 to 2.17)	1.01 (0.800 to 1.08)	3.04 (1.08 to 5.00)		

TNO155 + ribociclib (ROW)

	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1_ROW	TNO155 20mg QD 2/1 + ribo 200mg QD cont_ROW	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1_ROW	TNO155 40mg QD + ribo 200mg QD combined_ROW	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1_ROW	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1_ROW	TNO155 60mg QD 2/1 + ribo 200mg QD cont_ROW
Arm/Group Description	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous, 2w on/1w off and 3w on/1w off)	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous
Number of Participants Analyzed [units: participants]	4	3	5	13	3	0	3
Time to maximum observed plasma concentration (Tmax) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	1.53 (1.00 to 3.95)	0.983 (0 to 2.00)	2.12 (1.00 to 7.07)	2.00 (0.950 to 7.07)	3.97 (0.967 to 4.00)		2.00 (1.03 to 2.00)

NOVARTIS

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients)

Description	PK parameters were calculated based on TNO155 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 (TNO155+ribociclib only), 5 (TNO155+spartalizumab only) and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received TNO155 in combination with spartalizumab or ribociclib and had an available value for the outcome measure. For TNO155 plus ribociclib, only patients from rest of world (ROW) excluding Japan are considered for this endpoint. PAS consisted of all patients who provided an evaluable PK profile.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	4	12	6	3	4	4	2	0	0
Area under the plasma concentration-time curve	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**

from time zero to the time of the last quantifiable concentration (AUClast) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (units: hr*ng/mL)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)
	920 (35.7%)	2640 (33.8%)	372 (32.6%)	679 (32.5%)	1080 (47.2%)	1720 (51.6%)	4690 (28.0%)		

TNO155 + ribociclib (ROW)

	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1_ROW	TNO155 20mg QD 2/1 + ribo 200mg QD cont_ROW	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1_ROW	TNO155 40mg QD + ribo 200mg QD combined_ROW	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1_ROW	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1_ROW	TNO155 60mg QD 2/1 + ribo 200mg QD cont_ROW
Arm/Group Description	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous, 2w on/1w off and 3w on/1w off)	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous
Number of Participants Analyzed	4	3	5	13	3	0	3

[units: participants]							
Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of TNO155 – TNO155 plus spartalizumab and TNO155 plus ribociclib (ROW patients) (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	1160 (13.7%)	881 (9.7%)	2310 (18.5%)	1480 (65.1%)	2140 (34.5%)		2920 (26.8%)

Maximum observed plasma concentration (Cmax) of TNO155 – TNO155 plus ribociclib (Japan patients)

Description	PK parameters were calculated based on TNO155 plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from Japan in the pharmacokinetic analysis set (PAS) who received TNO155 plus ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 20mg QD + ribo 200mg QD combined_JP**	**TNO155 40mg QD + ribo 200mg QD combined_JP**

Arm/Group Description	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD (continuous and 2w on/1w off)	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous and 3w on/1w off)
Number of Participants Analyzed [units: participants]	1	3	5	5
Maximum observed plasma concentration (Cmax) of TNO155 – TNO155 plus ribociclib (Japan patients) (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	175	369 (23.8%)	171 (46.6%)	540 (24.0%)

Time to maximum observed plasma concentration (Tmax) of TNO155 – TNO155 plus ribociclib (Japan patients)

Description	PK parameters were calculated based on TNO155 plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) observed concentration following a dose. Actual sampling times were considered for the calculation of PK parameters.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from Japan in the pharmacokinetic analysis set (PAS) who received TNO155 plus ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 20mg QD + ribo 200mg QD combined_JP**	**TNO155 40mg QD + ribo 200mg QD combined_JP**
Arm/Group Description	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD (continuous and 2w on/1w off)	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous and 3w on/1w off)

Number of Participants Analyzed [units: participants]	1	3	5	5
Time to maximum observed plasma concentration (Tmax) of TNO155 – TNO155 plus ribociclib (Japan patients) (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	4.22 (4.22 to 4.22)	4.03 (2.13 to 4.22)	2.10 (1.98 to 4.08)	4.10 (2.02 to 7.93)

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of TNO155 – TNO155 plus ribociclib (Japan patients)

Description	PK parameters were calculated based on TNO155 plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from Japan in the pharmacokinetic analysis set (PAS) who received TNO155 plus ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 20mg QD + ribo 200mg QD combined_JP**	**TNO155 40mg QD + ribo 200mg QD combined_JP**
Arm/Group Description	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD (continuous and 2w on/1w off)	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous and 3w on/1w off)
Number of Participants Analyzed [units: participants]	1	3	5	5
Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of TNO155 – TNO155 plus ribociclib (Japan	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**

patients) (units: hr*ng/mL)				
	1220	2410 (31.3%)	973 (52.3%)	3530 (27.0%)

Maximum observed serum concentration (Cmax) of spartalizumab

Description	PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	Cycle 1: pre-dose, 1, 144 and 312 hours after the end of the infusion. The duration of the infusion was 30 minutes. One cycle=21 days
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received spartalizumab and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	4	18	6	5	4	6	6	2	0
Maximum observed serum concentratio	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**	**Geometric Mean (Geometric**

n (Cmax) of spartalizumab (units: µg/mL)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)	Coefficient of Variation)
	84.2 (25.7%)	74.3 (38.7%)	73.5 (39.0%)	68.6 (24.6%)	76.9 (14.7%)	84.3 (25.2%)	78.0 (33.9%)	92.4 (11.3%)	

Time to maximum observed serum concentration (Tmax) of spartalizumab

Description	PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) observed concentration following a dose. Actual sampling times were considered for the calculation of PK parameters.
Time Frame	Cycle 1: pre-dose, 1, 144 and 312 hours after the end of the infusion. The duration of the infusion was 30 minutes. One cycle=21 days
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received spartalizumab and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	4	18	6	5	4	6	6	2	0

Time to maximum observed serum concentration (Tmax) of spartalizumab (units: hours)	Median (Full Range)	Median (Full Range)	Median (Full Range)	Median (Full Range)	Median (Full Range)	Median (Full Range)	Median (Full Range)	Median (Full Range)	Median (Full Range)
	1.57 (0 to 2.18)	1.61 (0 to 2.13)	2.04 (1.55 to 142)	1.73 (1.55 to 2.28)	1.54 (1.25 to 2.07)	1.63 (1.30 to 2.05)	1.57 (0.550 to 2.02)	1.11 (0.583 to 1.63)	

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

Description	PK parameters were calculated based on spartalizumab serum concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.
Time Frame	Cycle 1: pre-dose, 1, 144 and 312 hours after the end of the infusion. The duration of the infusion was 30 minutes. One cycle=21 days
Analysis Population Description	Patients in the pharmacokinetic analysis set (PAS) who received spartalizumab and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	TNO155 60mg QD 2/1 + sparta 300mg Q3W	TNO155 5mg BID 2/1 + sparta 300mg Q3W	TNO155 10mg BID 2/1 + sparta 300mg Q3W	TNO155 20mg BID 2/1 + sparta 300mg Q3W	TNO155 30mg BID 2/1 + sparta 300mg Q3W	TNO155 40mg BID 2/1 + sparta 300mg Q3W	TNO155 50mg BID 2/1 + sparta 300mg Q3W	TNO155 60mg BID 2/1 + sparta 300mg Q3W
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral QD 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 5 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 10 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 20 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 30 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 40 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 50 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W	TNO155 60 mg oral BID 2w on/1w off in combination with spartalizumab 300 mg IV Q3W

Number of Participants Analyzed [units: participants]	4	18	6	5	4	6	6	2	0
Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of spartalizumab (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)**
	8580 (95.2%)	10600 (34.0%)	12900 (23.3%)	9760 (32.7%)	11400 (22.9%)	11700 (26.4%)	10000 (41.7%)	9090 (8.0%)	

Maximum observed plasma concentration (Cmax) of ribociclib – ROW patients

Description	PK parameters were calculated based on ribociclib plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from rest of world (ROW) excluding Japan in the pharmacokinetic analysis set (PAS) who received TNO155 in combination ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 20mg BID 3/1 + ribo	**TNO155 20mg QD 2/1 + ribo**	**TNO155 30mg BID 3/1 + ribo**	**TNO155 40mg QD + ribo 200mg**	**TNO155 40mg QD 3/1 + ribo**	**TNO155 40mg BID 3/1 + ribo**	**TNO155 60mg QD 2/1 + ribo**

	150mg QD 3/1_ROW	200mg QD cont_ROW	200mg QD 3/1_ROW	QD combined_ROW	150mg QD 3/1_ROW	200mg QD 3/1_ROW	200mg QD cont_ROW
Arm/Group Description	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous, 2w on/1w off and 3w on/1w off)	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous
Number of Participants Analyzed [units: participants]	4	3	5	13	3	0	3
Maximum observed plasma concentration (Cmax) of ribociclib – ROW patients (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	198 (54.5%)	808 (17.5%)	435 (45.3%)	708 (99.9%)	547 (225.7%)		689 (26.0%)

Time to maximum observed plasma concentration (Tmax) of ribociclib – ROW patients

Description	PK parameters were calculated based on ribociclib plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) observed concentration following a dose. Actual sampling times were considered for the calculation of PK parameters.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from rest of world (ROW) excluding Japan in the pharmacokinetic analysis set (PAS) who received TNO155 in combination ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 20mg BID 3/1 + ribo	TNO155 20mg QD 2/1 + ribo	TNO155 30mg BID 3/1 + ribo	TNO155 40mg QD + ribo 200mg	TNO155 40mg QD 3/1 + ribo	TNO155 40mg BID 3/1 + ribo	TNO155 60mg QD 2/1 + ribo

	150mg QD 3/1_ROW	200mg QD cont_ROW	200mg QD 3/1_ROW	QD combined_ROW	150mg QD 3/1_ROW	200mg QD 3/1_ROW	200mg QD cont_ROW
Arm/Group Description	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous, 2w on/1w off and 3w on/1w off)	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous
Number of Participants Analyzed [units: participants]	4	3	5	13	3	0	3
Time to maximum observed plasma concentration (Tmax) of ribociclib – ROW patients (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	1.53 (1.00 to 3.95)	0.983 (0.950 to 2.00)	2.12 (2.00 to 4.15)	2.00 (0.950 to 7.07)	3.97 (0.967 to 4.00)		2.00 (2.00 to 2.13)

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of ribociclib – ROW patients

Description	PK parameters were calculated based on ribociclib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from rest of world (ROW) excluding Japan in the pharmacokinetic analysis set (PAS) who received TNO155 in combination ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 20mg BID 3/1 + ribo	TNO155 20mg QD 2/1 + ribo	TNO155 30mg BID 3/1 + ribo	TNO155 40mg QD + ribo 200mg	TNO155 40mg QD 3/1 + ribo	TNO155 40mg BID 3/1 + ribo	TNO155 60mg QD 2/1 + ribo

	150mg QD 3/1_ROW	200mg QD cont_ROW	200mg QD 3/1_ROW	QD combined_ROW	150mg QD 3/1_ROW	200mg QD 3/1_ROW	200mg QD cont_ROW
Arm/Group Description	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous, 2w on/1w off and 3w on/1w off)	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg oral QD 3w on/1w off	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD continuous
Number of Participants Analyzed [units: participants]	4	3	5	13	3	0	3
Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of ribociclib – ROW patients (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	1070 (64.3%)	3450 (34.8%)	2140 (47.5%)	3210 (92.2%)	2760 (216.9%)		3350 (22.1%)

Maximum observed plasma concentration (Cmax) of ribociclib – Japan patients

Description	PK parameters were calculated based on ribociclib plasma concentrations by using non-compartmental methods. Cmax is defined as the maximum (peak) observed concentration following a dose.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from Japan in the pharmacokinetic analysis set (PAS) who received TNO155 plus ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP	TNO155 20mg QD + ribo 200mg QD combined_JP	TNO155 40mg QD + ribo 200mg QD combined_JP
Arm/Group Description	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD (continuous and 2w on/1w off)	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous and 3w on/1w off)
Number of Participants Analyzed [units: participants]	1	3	5	5
Maximum observed plasma concentration (Cmax) of ribociclib – Japan patients (units: ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	658	486 (50.5%)	702 (46.2%)	770 (18.9%)

Time to maximum observed plasma concentration (Tmax) of ribociclib – Japan patients

Description	PK parameters were calculated based on ribociclib plasma concentrations by using non-compartmental methods. Tmax is defined as the time to reach maximum (peak) observed concentration following a dose. Actual sampling times were considered for the calculation of PK parameters.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from Japan in the pharmacokinetic analysis set (PAS) who received TNO155 plus ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP	TNO155 20mg QD + ribo 200mg QD combined_JP	TNO155 40mg QD + ribo 200mg QD combined_JP
Arm/Group Description	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg

			(continuous and 2w on/1w off)	oral QD (continuous and 3w on/1w off)
Number of Participants Analyzed [units: participants]	1	3	5	5
Time to maximum observed plasma concentration (Tmax) of ribociclib – Japan patients (units: hours)	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**	**Median (Full Range)**
	7.42 (7.42 to 7.42)	4.22 (2.15 to 7.03)	2.10 (1.98 to 4.08)	3.98 (2.07 to 4.00)

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of ribociclib – Japan patients

Description	PK parameters were calculated based on ribociclib plasma concentrations by using non-compartmental methods. The linear trapezoidal method was used for AUC calculation.
Time Frame	Cycle 1 Day 14 (C1D14): pre-dose, 1, 2, 4 and 8 hours after the morning dose. One cycle=21 or 28 days, depending on the dosing schedule.
Analysis Population Description	Patients from Japan in the pharmacokinetic analysis set (PAS) who received TNO155 plus ribociclib and had an available value for the outcome measure. PAS consisted of all patients who provided an evaluable PK profile.

	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_JP	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_JP**	**TNO155 20mg QD + ribo 200mg QD combined_JP**	**TNO155 40mg QD + ribo 200mg QD combined_JP**
Arm/Group Description	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg oral QD 3w on/1w off	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg oral QD (continuous and 2w on/1w off)	TNO155 40 mg oral QD (2w on/1w off and 3w on/1w off) in combination with ribociclib 200 mg oral QD (continuous and 3w on/1w off)
Number of Participants Analyzed [units: participants]	1	3	5	5

Area under the plasma concentration-time curve from time zero to the time of the last quantifiable concentration (AUClast) of ribociclib – Japan patients (units: hr*ng/mL)	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**	**Geometric Mean (Geometric Coefficient of Variation)**
	3910	2600 (52.7%)	3450 (45.0%)	4700 (21.7%)

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 treatment to 150 days after last dose of TNO155+spartalizumab and 30 days after last dose of TNO155+ribociclib. Survival FU deaths were collected from 151 days after last dose of TNO155+spartalizumab and 31 days after last dose of TNO155+ribociclib 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 post-treatment safety FU deaths: up to approximately 2.1 years (TNO155+spartalizumab) and 1.5 years (TNO155+ribociclib). Survival FU deaths: up to approximately 3.7 years (TNO155+spartalizumab) and 2.4 years (TNO155+ribociclib)
Analysis Population Description	All patients who received at least one dose of any study treatment.

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W	**TNO155 60mg QD 2/1 + sparta 300mg Q3W**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off	TNO155 60 mg oral QD 2w on/1w off	TNO155 5 mg oral BID 2w on/1w off	TNO155 10 mg oral BID 2w on/1w off	TNO155 20 mg oral BID 2w on/1w off	TNO155 30 mg oral BID 2w on/1w off	TNO155 40 mg oral BID 2w on/1w off	TNO155 50 mg oral BID 2w on/1w off	TNO155 60 mg oral BID 2w on/1w off

	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W	in combination with spartalizumab 300 mg IV Q3W
Number of Participants Analyzed [units: participants]	5	19	6	5	5	6	7	3	1
On-treatment and post-treatment safety FU deaths (n=5,19,6,5,5,6,7,3,1,5,8,5,4,8,1,5,4,9,1,6,9)	2	8	2	3	1	3	5	1	1
Survival FU deaths (n=3,11,4,2,4,3,2,2,0,5,8,5,3,6,1,5,4,8,0,6,9)	1	4	4	1	2	2	2	2	
All deaths (n=5,19,6,5,5,6,7,3,1,5,8,5,4,8,1,5,4,9,1,6,9)	3	12	6	4	3	5	7	3	1

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont	**TNO155 40mg QD 2/1 + ribo 200mg QD cont**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1**
Arm/Group Description	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg	TNO155 60 mg oral QD 2w on/1w off in combination with ribociclib 200 mg	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 150 mg	TNO155 40 mg oral QD 3w on/1w off in combination with ribociclib 200 mg	TNO155 10 mg oral BID 3w on/1w off in combination with ribociclib 200 mg	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 150 mg	TNO155 20 mg oral BID 3w on/1w off in combination with ribociclib 200 mg	TNO155 30 mg oral BID 3w on/1w off in combination with ribociclib 200 mg	TNO155 40 mg oral BID 3w on/1w off in combination with ribociclib 200 mg	TNO155 20 mg oral QD 2w on/1w off in combination with ribociclib 200 mg	TNO155 40 mg oral QD 2w on/1w off in combination with ribociclib 200 mg

	oral QD continuous	oral QD continuous	oral QD continuous	oral QD 3w on/1w off	oral QD 3w on/1w off	oral QD 3w on/1w off	oral QD 3w on/1w off	oral QD 3w on/1w off	oral QD 3w on/1w off	oral QD 3w on/1w off	oral QD 2w on/1w off	oral QD 2w on/1w off
Number of Participants Analyzed [units: participants]	5	8	5	4	8	1	5	4	9	1	6	9
On-treatment and post-treatment safety FU deaths	0	0	0	1	2	0	0	0	1	1	0	0
Survival FU deaths	5	8	4	3	3	1	5	2	6		4	3
All deaths	5	8	4	4	5	1	5	2	7	1	4	3

Safety Results

Time Frame	On- and post-treatment safety FU: from first dose of study treatment to 150 days after last dose of TNO155+spartalizumab and 30 days after last dose of TNO155+ribociclib, up to approx. 2.1 years (TNO155+spartalizumab) and 1.5 years (TNO155+ribociclib). Deaths in survival period: from 151 days after last dose of TNO155+spartalizumab and 31 days after last dose of TNO155+ribociclib until end of study, up to approx. 3.7 years (TNO155+spartalizumab) and 2.4 years (TNO155+ribociclib).
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)

NOVARTIS

Collection Approach for Table Default Systematic Assessment

All-Cause Mortality

TNO155 + spartalizumab – Safety data up to 150 days after last dose

	TNO155 20mg QD 2/1 + sparta 300mg Q3W N = 5	TNO155 60mg QD 2/1 + sparta 300mg Q3W N = 19	TNO155 5mg BID 2/1 + sparta 300mg Q3W N = 6	TNO155 10mg BID 2/1 + sparta 300mg Q3Wd N = 5	TNO155 20mg BID 2/1 + sparta 300mg Q3W N = 5	TNO155 30mg BID 2/1 + sparta 300mg Q3W N = 6	TNO155 40mg BID 2/1 + sparta 300mg Q3W N = 7	TNO155 50mg BID 2/1 + sparta 300mg Q3W N = 3	TNO155 60mg BID 2/1 + sparta 300mg Q3W N = 1
Arm/Group Description	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab
Total Number Affected	2	8	2	3	1	3	5	1	1
Total Number At Risk	5	19	6	5	5	6	7	3	1

TNO155 + ribociclib – Safety data up to 30 days after last dose

	TNO155 20mg QD 2/1 + ribo 200mg QD cont N = 5	TNO155 40mg QD 2/1 + ribo 200mg QD cont N = 8	TNO155 60mg QD 2/1 + ribo 200mg QD cont N = 5	TNO155 40mg QD 3/1 + ribo 150mg QD 3/1 N = 4	TNO155 40mg QD 3/1 + ribo 200mg QD 3/1 N = 8	TNO155 10mg BID 3/1 + ribo 200mg QD 3/1 N = 1	TNO155 20mg BID 3/1 + ribo 150mg QD 3/1 N = 5	TNO155 20mg BID 3/1 + ribo 200mg QD 3/1 N = 4	TNO155 30mg BID 3/1 + ribo 200mg QD 3/1 N = 9	TNO155 40mg BID 3/1 + ribo 200mg QD 3/1 N = 1	TNO155 20mg QD 2/1 + ribo 200mg QD 2/1 N = 6	TNO155 40mg QD 2/1 + ribo 200mg QD 2/1 N = 9
Arm/ Group Description	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib	Safety data up to 30 days after last dose of TNO155+ ribociclib
Total Number Affected	0	0	0	1	2	0	0	0	1	1	0	0
Total Number At Risk	5	8	5	4	8	1	5	4	9	1	6	9

TNO155 + spartalizumab – Survival Follow-Up

	TNO155 20mg QD 2/1 + sparta 300mg Q3W_Survival period N = 3	TNO155 60mg QD 2/1 + sparta 300mg Q3W_Survival period N = 11	TNO155 5mg BID 2/1 + sparta 300mg Q3W_Survival period N = 4	TNO155 10mg BID 2/1 + sparta 300mg Q3W_Survival period N = 2	TNO155 20mg BID 2/1 + sparta 300mg Q3W_Survival period N = 4	TNO155 30mg BID 2/1 + sparta 300mg Q3W_Survival period N = 3	TNO155 40mg BID 2/1 + sparta 300mg Q3W_Survival period N = 2	TNO155 50mg BID 2/1 + sparta 300mg Q3W_Survival period N = 2	TNO155 60mg BID 2/1 + sparta 300mg Q3W_Survival period N = 0
Arm/Group Description	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up	Deaths collected in the survival follow-up

	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.	period (starting from Day 151 after last dose of TNO155+spartalizumab). No AEs were collected during this period.
Total Number Affected	1	4	4	1	2	2	2	2	0
Total Number At Risk	3	11	4	2	4	3	2	2	0

TNO155 + ribociclib – Survival Follow-Up

	TNO155 20mg QD 2/1 + ribo 200mg QD cont_Survival period N = 5	**TNO155 40mg QD 2/1 + ribo 200mg QD cont_Survival period N = 8**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont_Survival period N = 5**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1_Survival period N = 3**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1_Survival period N = 6**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1_Survival period N = 1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1_Survival period N = 5**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1_Survival period N = 4**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1_Survival period N = 8**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1_Survival period N = 0**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1_Survival period N = 6**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1_Survival period N = 9**
Arm/Group Desc	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period	Deaths collected in the survival follow-up period

riptio n	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.	(starting from Day 31 after last dose of TNO155+ ribociclib) . No AEs were collected during this period.
Total Number Affected	5	8	4	3	3	1	5	2	6	0	4	3
Total Number At Risk	5	8	5	3	6	1	5	4	8	0	6	9

Serious Adverse Events

Time Frame	On- and post-treatment safety FU: from first dose of study treatment to 150 days after last dose of TNO155+spartalizumab and 30 days after last dose of TNO155+ribociclib, up to approx. 2.1 years (TNO155+spartalizumab) and 1.5 years (TNO155+ribociclib). Deaths in survival period: from 151 days after last dose of TNO155+spartalizumab and 31 days after last dose of TNO155+ribociclib until end of study, up to approx. 3.7 years (TNO155+spartalizumab) and 2.4 years (TNO155+ribociclib).
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

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W N = 5	**TNO155 60mg QD 2/1 + sparta 300mg Q3W N = 19**	**TNO155 5mg BID 2/1 + sparta 300mg Q3W N = 6**	**TNO155 10mg BID 2/1 + sparta 300mg Q3W N = 5**	**TNO155 20mg BID 2/1 + sparta 300mg Q3W N = 5**	**TNO155 30mg BID 2/1 + sparta 300mg Q3W N = 6**	**TNO155 40mg BID 2/1 + sparta 300mg Q3W N = 7**	**TNO155 50mg BID 2/1 + sparta 300mg Q3W N = 3**	**TNO155 60mg BID 2/1 + sparta 300mg Q3W N = 1**
Arm/Group Description	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab
Total # Affected by any Serious Adverse Event	2	12	3	3	4	4	6	2	1
Total # at Risk by any Serious Adverse Event	5	19	6	5	5	6	7	3	1
Blood and lymphatic									

system disorders									
Anaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Febrile neutropenia	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%)
Myelosuppression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders									
Acute 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%)
Pericardial effusion	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%)
Endocrine disorders									
Adrenal insufficiency	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders									
Anal fistula	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diarrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Gastric haemorrhage	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorder	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	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%)
Oesophageal perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Oesophageal varices haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Rectal haemorrhage	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%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (33.33%)	0 (0.00%)
Vomiting	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
General disorders and administrat									

ion site conditions									
Localised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	1 (20.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)
Hepatobiliary disorders									
Cholangitis	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%)
Hyperbilirubinaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders									
Cytokine release syndrome	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%)
Hypersensitivity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations									
Bacteraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchitis	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

COVID-19 pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dengue fever	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Empyema	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	4 (21.05%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Pneumonia aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural infection	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyelonephritis	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract infection	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urosepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications									

Accidental overdose	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Femur fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tracheal obstruction	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations									
Blood bilirubin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatinine increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ejection fraction decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urine output decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
White blood cell count	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

decreased									
Metabolism and nutrition disorders									
Hypokalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malnutrition	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Type 1 diabetes mellitus	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%)
Musculoskeletal and connective tissue disorders									
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	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%)
Rhabdomyolysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)									
Tumour haemorrhage	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Nervous system disorders									
Autoimmune encephalopathy	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Central nervous system vasculitis	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%)
Dysarthria	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic encephalopathy	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ischaemic stroke	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders									
Acute kidney injury	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hydronephrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Renal vasculitis	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%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Urinary tract	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)

obstruction									
Respiratory, thoracic and mediastinal disorders									
Acute respiratory failure	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	1 (100.00%)
Laryngeal oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pharyngeal haemorrhage	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonitis	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%)
Pneumothorax	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%)
Pulmonary embolism	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%)
Pulmonary oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders									

Cutaneous vasculitis	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%)
Vascular disorders									
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%)

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont N = 5	**TNO155 40mg QD 2/1 + ribo 200mg QD cont N = 8**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont N = 5**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1 N = 4**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1 N = 8**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1 N = 1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1 N = 5**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1 N = 4**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1 N = 9**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1 N = 1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1 N = 6**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1 N = 9**
Arm/Group Description	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib
Total # Affected by any Serious Adverse Event	2	4	2	3	2	1	2	0	4	1	2	5
Total # at Risk by any Serious	5	8	5	4	8	1	5	4	9	1	6	9

Adverse Event												
Blood and lymphatic system disorders												
Anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myelosuppression	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders												
Acute myocardial infarction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pericardial effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endocrine disorders												
Adrenal insufficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)
Gastrointestinal disorders												

Anal fistula	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)	0 (0.00%)	0 (0.00%)
Diarrhoea	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastric 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%)	0 (0.00%)
Gastrointestinal 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%)
Gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (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%)
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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oesophageal perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oesophageal varices 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%)	0 (0.00%)
Rectal haemorrhage	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Small intestinal obstruction	0 (0.00%)	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%)
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%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions												
Localised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
Pyrexia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	2 (22.22%)
Hepatobiliary disorders												
Cholangitis	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperbilirubinaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders												
Cytokine release syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hypersensitivity	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations												
Bacteraemia	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
COVID-19 pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Dengue fever	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
Empyema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Post procedural infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyelonephritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)
Urinary tract infection	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urosepsis	0 (0.00%)	1 (12.50%)	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%)
Injury, poisoning and procedural complications												
Accidental overdose	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Femur fracture	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tracheal obstruction	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%)
Investigations												
Blood bilirubin increased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Blood creatinine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ejection fraction decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	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 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urine output decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
White blood cell count decreased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders												
Hypokalaemia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malnutrition	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Type 1 diabetes mellitus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders												
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (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%)
Rhabdomyolysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)												
Tumour 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%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders												
Autoimmune encephalopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Central nervous system vasculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysarthria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic encephalopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ischaemic stroke	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders												
Acute kidney injury	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hydronephrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal vasculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders												

Acute respiratory failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Laryngeal oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Pharyngeal 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%)	0 (0.00%)
Pleural effusion	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Pneumonitis	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Pneumothorax	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary oedema	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders												
Cutaneous vasculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders												

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%)	0 (0.00%)	1 (11.11%)

Other (Not Including Serious) Adverse Events

Time Frame	On- and post-treatment safety FU: from first dose of study treatment to 150 days after last dose of TNO155+spartalizumab and 30 days after last dose of TNO155+ribociclib, up to approx. 2.1 years (TNO155+spartalizumab) and 1.5 years (TNO155+ribociclib). Deaths in survival period: from 151 days after last dose of TNO155+spartalizumab and 31 days after last dose of TNO155+ribociclib until end of study, up to approx. 3.7 years (TNO155+spartalizumab) and 2.4 years (TNO155+ribociclib).
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%

TNO155 + spartalizumab

	TNO155 20mg QD 2/1 + sparta 300mg Q3W N = 5	TNO155 60mg QD 2/1 + sparta 300mg Q3W N = 19	TNO155 5mg BID 2/1 + sparta 300mg Q3W N = 6	TNO155 10mg BID 2/1 + sparta 300mg Q3W N = 5	TNO155 20mg BID 2/1 + sparta 300mg Q3W N = 5	TNO155 30mg BID 2/1 + sparta 300mg Q3W N = 6	TNO155 40mg BID 2/1 + sparta 300mg Q3W N = 7	TNO155 50mg BID 2/1 + sparta 300mg Q3W N = 3	TNO155 60mg BID 2/1 + sparta 300mg Q3W N = 1

Arm/Group Description	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab	Safety data up to 150 days after last dose of TNO155+spartalizumab
Total # Affected by any Other Adverse Event	5	18	6	5	5	6	6	3	1
Total # at Risk by any Other Adverse Event	5	19	6	5	5	6	7	3	1
Blood and lymphatic system disorders									
Anaemia	1 (20.00%)	5 (26.32%)	1 (16.67%)	2 (40.00%)	2 (40.00%)	1 (16.67%)	4 (57.14%)	0 (0.00%)	0 (0.00%)
Eosinophilia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Febrile neutropenia	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%)
Hyperleukocytosis	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iron deficiency anaemia	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%)
Leukopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymph node pain	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%)
Lymphopenia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Myelosuppression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	0 (0.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Pancytopenia	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%)
Thrombocytopenia	0 (0.00%)	3 (15.79%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Cardiac disorders									
Atrioventricular block first degree	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%)
Bundle branch block right	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%)
Cardiac failure	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Palpitations	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pericardial effusion	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sinus tachycardia	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Tricuspid valve disease	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ventricular extrasystoles	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear and labyrinth disorders									

Deafness unilateral	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear pain	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Middle ear effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tympanic membrane perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Endocrine disorders									
Adrenal insufficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypothyroidism	0 (0.00%)	2 (10.53%)	1 (16.67%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Parathyroid disorder	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye disorders									
Blepharitis	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%)
Dry eye	1 (20.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eyelid oedema	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Keratitis	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%)
Lacrimation increased	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%)
Periorbital oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vision blurred	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Visual impairment	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%)

Gastrointestinal disorders									
Abdominal distension	0 (0.00%)	1 (5.26%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ascites	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Cheilitis	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	1 (20.00%)	2 (10.53%)	3 (50.00%)	1 (20.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diarrhoea	2 (40.00%)	7 (36.84%)	1 (16.67%)	2 (40.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	1 (100.00%)
Dry mouth	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Dyspepsia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Dysphagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Epigastric discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Glossodynia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemorrhoidal 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%)
Haemorrhoids	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)

Large intestinal obstruction	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%)
Melaena	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mouth haemorrhage	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mouth ulceration	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%)
Nausea	2 (40.00%)	1 (5.26%)	2 (33.33%)	0 (0.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	1 (33.33%)	0 (0.00%)
Odynophagia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oesophagitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oral pain	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rectal haemorrhage	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Stomatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tongue oedema	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper gastrointestinal haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vomiting	3 (60.00%)	1 (5.26%)	2 (33.33%)	0 (0.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
General disorders and administratio									

n site conditions									
Asthenia	0 (0.00%)	6 (31.58%)	1 (16.67%)	1 (20.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Axillary 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%)
Chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Face oedema	0 (0.00%)	6 (31.58%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	2 (40.00%)	1 (5.26%)	2 (33.33%)	0 (0.00%)	1 (20.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Generalised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion site extravasation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Malaise	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mucosal inflammation	0 (0.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oedema peripheral	0 (0.00%)	6 (31.58%)	1 (16.67%)	0 (0.00%)	2 (40.00%)	1 (16.67%)	3 (42.86%)	1 (33.33%)	0 (0.00%)
Pain	0 (0.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral swelling	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%)
Pyrexia	0 (0.00%)	3 (15.79%)	1 (16.67%)	2 (40.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Swelling face	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%)
Hepatobiliary disorders									
Cholangitis	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Cholestasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic cytolysis	1 (20.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic pain	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%)
Hypertransaminasaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Jaundice	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%)
Ocular icterus	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders									
Hypersensitivity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations									
Biliary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Clostridium difficile colitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Conjunctivitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fungal 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%)
Herpes zoster	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Impetigo	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Localised infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peritonitis	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	3 (15.79%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract infection	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	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%)
Urinary tract infection bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vulvovaginal mycotic infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications									
Contusion	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immunisation reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Ligament sprain	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%)
Medication error	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Overdose	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)
Procedural pain	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Road traffic accident	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin laceration	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%)
Investigations									
Activated partial thromboplastin time prolonged	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%)
Alanine aminotransferase increased	1 (20.00%)	11 (57.89%)	0 (0.00%)	1 (20.00%)	3 (60.00%)	1 (16.67%)	3 (42.86%)	2 (66.67%)	1 (100.00%)
Alpha hydroxybutyrate dehydrogenase increased	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%)
Amylase increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Aspartate aminotransferase increased	2 (40.00%)	11 (57.89%)	0 (0.00%)	1 (20.00%)	2 (40.00%)	3 (50.00%)	4 (57.14%)	2 (66.67%)	1 (100.00%)
Bilirubin conjugated increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood albumin decreased	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood alkaline phosphatase increased	1 (20.00%)	2 (10.53%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood bilirubin increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	1 (20.00%)	1 (20.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine 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%)
Blood creatine phosphokinase increased	0 (0.00%)	9 (47.37%)	2 (33.33%)	2 (40.00%)	2 (40.00%)	3 (50.00%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase MB 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%)
Blood creatinine increased	1 (20.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Blood glucose increased	0 (0.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Blood lactate dehydrogenase increased	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%)
Blood magnesium decreased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood potassium decreased	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood urea 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%)
Blood uric acid increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Body temperature increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Brain natriuretic peptide increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ejection fraction decreased	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Electrocardiogram ST segment depression	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Fibrin D dimer increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gamma-glutamyltransferase increased	1 (20.00%)	3 (15.79%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
International normalised ratio increased	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	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%)
Lymphocyte count decreased	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	1 (33.33%)	0 (0.00%)
N-terminal prohormone brain natriuretic peptide increased	1 (20.00%)	6 (31.58%)	2 (33.33%)	3 (60.00%)	1 (20.00%)	1 (16.67%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Nutritional condition abnormal	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Occult blood positive	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%)
Platelet count decreased	0 (0.00%)	5 (26.32%)	1 (16.67%)	0 (0.00%)	3 (60.00%)	1 (16.67%)	2 (28.57%)	0 (0.00%)	0 (0.00%)

SARS-CoV-2 test negative	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thyroxine free increased	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thyroxine increased	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Troponin I 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%)
Troponin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)
Troponin T increased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Weight decreased	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Weight increased	0 (0.00%)	4 (21.05%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
White blood cell count 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%)
White blood cells urine 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%)	0 (0.00%)
Metabolism and nutrition disorders									
Decreased appetite	0 (0.00%)	2 (10.53%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dehydration	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrolyte imbalance	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gout	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%)

Hypercalcaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperglycaemia	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperphosphataemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertriglyceridaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperuricaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoalbuminaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Hypocalcaemia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	0 (0.00%)	2 (10.53%)	1 (16.67%)	0 (0.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hypomagnesaemia	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hypophosphataemia	0 (0.00%)	4 (21.05%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoproteinaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iron deficiency	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%)
Metabolic acidosis	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%)
Musculoskeletal and									

connective tissue disorders									
Arthralgia	0 (0.00%)	4 (21.05%)	1 (16.67%)	0 (0.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	2 (66.67%)	0 (0.00%)
Arthritis	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	1 (20.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bursitis	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%)
Joint stiffness	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Limb discomfort	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscular weakness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	0 (0.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myositis	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%)
Osteonecrosis of jaw	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)
Shoulder girdle pain	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Synovitis	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%)
Trismus	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified									

(incl cysts and polyps)									
Tumour associated fever	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour haemorrhage	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nervous system disorders									
Akathisia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aphasia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysarthria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysdiadochokinesis	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%)
Dysgeusia	0 (0.00%)	2 (10.53%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (42.86%)	0 (0.00%)	0 (0.00%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lethargy	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%)
Medullary compression syndrome	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neuropathy peripheral	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paraesthesia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral sensory neuropathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Product issues									
Device dislocation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders									
Anxiety	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Confusional state	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%)
Insomnia	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders									
Choluria	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysuria	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Micturition frequency decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pollakiuria	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%)
Renal failure	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders									
Benign prostatic hyperplasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Dysmenorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Perineal pain	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%)
Scrotal oedema	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%)
Respiratory, thoracic and mediastinal disorders									
Aphonia	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspiration	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchial obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cough	1 (20.00%)	3 (15.79%)	1 (16.67%)	0 (0.00%)	1 (20.00%)	1 (16.67%)	2 (28.57%)	0 (0.00%)	0 (0.00%)
Dry throat	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	1 (20.00%)	2 (10.53%)	1 (16.67%)	0 (0.00%)	2 (40.00%)	1 (16.67%)	0 (0.00%)	1 (33.33%)	1 (100.00%)
Dyspnoea exertional	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%)
Epistaxis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemoptysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hiccups	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoxia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Laryngeal oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lung consolidation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Nasal congestion	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasal inflammation	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pharyngeal inflammation	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Pleurisy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
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%)	0 (0.00%)
Productive cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pulmonary embolism	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%)
Rhinorrhoea	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders									
Alopecia	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%)
Dermatitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dermatitis acneiform	0 (0.00%)	3 (15.79%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (33.33%)	1 (100.00%)
Dry skin	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eczema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (14.29%)	0 (0.00%)	0 (0.00%)

Night sweats	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Palmar-plantar erythrodysaesthesia syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Petechiae	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pruritus	0 (0.00%)	1 (5.26%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash	1 (20.00%)	3 (15.79%)	1 (16.67%)	0 (0.00%)	1 (20.00%)	1 (16.67%)	1 (14.29%)	1 (33.33%)	0 (0.00%)
Rash macular	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%)
Rash maculo-papular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash pruritic	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%)
Skin exfoliation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)	0 (0.00%)
Skin lesion	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin ulcer	0 (0.00%)	1 (5.26%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Umbilical 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%)
Vascular disorders									
Embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hypertension	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (14.29%)	0 (0.00%)	0 (0.00%)
Hypotension	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%)
Jugular 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%)

Lymphoedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)

TNO155 + ribociclib

	TNO155 20mg QD 2/1 + ribo 200mg QD cont N = 5	**TNO155 40mg QD 2/1 + ribo 200mg QD cont N = 8**	**TNO155 60mg QD 2/1 + ribo 200mg QD cont N = 5**	**TNO155 40mg QD 3/1 + ribo 150mg QD 3/1 N = 4**	**TNO155 40mg QD 3/1 + ribo 200mg QD 3/1 N = 8**	**TNO155 10mg BID 3/1 + ribo 200mg QD 3/1 N = 1**	**TNO155 20mg BID 3/1 + ribo 150mg QD 3/1 N = 5**	**TNO155 20mg BID 3/1 + ribo 200mg QD 3/1 N = 4**	**TNO155 30mg BID 3/1 + ribo 200mg QD 3/1 N = 9**	**TNO155 40mg BID 3/1 + ribo 200mg QD 3/1 N = 1**	**TNO155 20mg QD 2/1 + ribo 200mg QD 2/1 N = 6**	**TNO155 40mg QD 2/1 + ribo 200mg QD 2/1 N = 9**
Arm/Group Description	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib	Safety data up to 30 days after last dose of TNO155 +ribociclib
Total # Affected by any Other Adverse Event	5	8	5	4	8	1	5	4	9	1	6	9
Total # at Risk by any Other Adverse Event	5	8	5	4	8	1	5	4	9	1	6	9
Blood and lymphatic system disorders												

Anaemia	1 (20.00 %)	1 (12.50 %)	4 (80.00 %)	2 (50.00 %)	3 (37.50 %)	1 (100.0 0%)	2 (40.00 %)	3 (75.00 %)	4 (44.44 %)	0 (0.00%)	4 (66.67 %)	3 (33.33 %)
Eosinophilia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperleukocytosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iron deficiency anaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leukopenia	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymph node 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%)
Lymphopenia	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	1 (12.50 %)	1 (100.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myelosuppression	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	0 (0.00%)	3 (37.50 %)	1 (20.00 %)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	2 (22.22 %)	0 (0.00%)	0 (0.00%)	1 (11.11 %)
Pancytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Thrombocytopenia	1 (20.00 %)	1 (12.50 %)	0 (0.00%)	1 (25.00 %)	3 (37.50 %)	0 (0.00%)	2 (40.00 %)	0 (0.00%)	3 (33.33 %)	1 (100.0 0%)	0 (0.00%)	2 (22.22 %)
Cardiac disorders												
Atrioventricular block first degree	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Bundle branch block right	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Palpitations	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pericardial effusion	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 (11.11%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Sinus tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tachycardia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tricuspid valve disease	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%)
Ventricular extrasystoles	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear and labyrinth disorders												
Deafness unilateral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ear 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%)
Middle ear effusion	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%)
Tympanic membrane perforation	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Endocrine disorders												
Adrenal insufficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)
Hypothyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Parathyroid 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%)
Eye disorders												
Blepharitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dry eye	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eyelid oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Keratitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lacrimation 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%)
Periorbital oedema	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vision blurred	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Visual impairment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders												
Abdominal distension	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Abdominal pain	1 (20.00 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (12.50 %)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11 %)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11 %)
Ascites	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cheilitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	1 (20.00 %)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	2 (25.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (33.33 %)	0 (0.00%)	1 (16.67 %)	3 (33.33 %)
Diarrhoea	0 (0.00%)	1 (12.50 %)	3 (60.00 %)	2 (50.00 %)	2 (25.00 %)	0 (0.00%)	2 (40.00 %)	2 (50.00 %)	3 (33.33 %)	0 (0.00%)	1 (16.67 %)	3 (33.33 %)
Dry mouth	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspepsia	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysphagia	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%)
Epigastric discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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 %)
Gastritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22 %)
Gastrooesophageal reflux disease	0 (0.00%)	2 (25.00 %)	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%)
Glossodynia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemorrhoidal haemorrhage	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Haemorrhoids	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Large intestinal obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Melaena	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mouth haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mouth ulceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (25.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	2 (22.22%)
Odynophagia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oesophagitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
Oral pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rectal haemorrhage	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Small intestinal obstruction	0 (0.00%)	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%)
Stomatitis	1 (20.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tongue oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper gastrointestinal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

haemorrhage												
Vomiting	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	2 (25.00%)	1 (100.00%)	1 (20.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
General disorders and administration site conditions												
Asthenia	0 (0.00%)	1 (12.50%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)
Axillary pain	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Face oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (12.50%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Generalised oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infusion site extravasation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malaise	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mucosal inflammation	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oedema	1 (20.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (11.11%)

Oedema peripheral	0 (0.00%)	3 (37.50%)	0 (0.00%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	3 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
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%)
Peripheral swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	1 (20.00%)	0 (0.00%)	2 (40.00%)	2 (50.00%)	2 (25.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	2 (22.22%)	0 (0.00%)	3 (50.00%)	2 (22.22%)
Swelling	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Swelling face	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cholestasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic cytolysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatic pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertransaminasaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Jaundice	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ocular icterus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immune system disorders												

Hypersensitivity	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations												
Biliary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)
Clostridium difficile colitis	0 (0.00%)	0 (0.00%)	0 (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%)
Conjunctivitis	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	0 (0.00%)	0 (0.00%)	0 (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 (22.22%)
Fungal infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Impetigo	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Localised infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peritonitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)
Skin infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	1 (11.11%)

Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Urinary tract infection bacterial	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vulvovaginal mycotic infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications												
Contusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Immunisation reaction	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%)
Infusion related reaction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ligament sprain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Medication error	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Overdose	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Procedural pain	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Road traffic accident	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin laceration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations												
Activated partial thromboplastin time prolonged	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Alanine aminotransferase increased	3 (60.00%)	4 (50.00%)	2 (40.00%)	2 (50.00%)	5 (62.50%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	3 (33.33%)	0 (0.00%)	3 (50.00%)	3 (33.33%)
Alpha hydroxybutyrate dehydrogenase 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%)
Amylase increased	0 (0.00%)	2 (25.00%)	1 (20.00%)	0 (0.00%)	2 (25.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspartate aminotransferase increased	4 (80.00%)	6 (75.00%)	4 (80.00%)	2 (50.00%)	5 (62.50%)	0 (0.00%)	2 (40.00%)	3 (75.00%)	4 (44.44%)	0 (0.00%)	2 (33.33%)	3 (33.33%)
Bilirubin conjugated 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%)
Blood albumin decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Blood alkaline phosphatase increased	2 (40.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood bilirubin increased	1 (20.00 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11 %)
Blood creatine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.0 0%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatine phosphokinase increased	3 (60.00 %)	5 (62.50 %)	3 (60.00 %)	2 (50.00 %)	4 (50.00 %)	0 (0.00%)	2 (40.00 %)	1 (25.00 %)	5 (55.56 %)	0 (0.00%)	2 (33.33 %)	1 (11.11 %)
Blood creatine phosphokinase MB increased	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%)
Blood creatinine increased	2 (40.00 %)	2 (25.00 %)	1 (20.00 %)	0 (0.00%)	2 (25.00 %)	0 (0.00%)	0 (0.00%)	2 (50.00 %)	2 (22.22 %)	0 (0.00%)	1 (16.67 %)	1 (11.11 %)
Blood glucose 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%)
Blood lactate dehydrogenase increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood magnesium decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11 %)

Blood potassium decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood urea increased	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood uric acid increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Body temperature 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%)
Brain natriuretic peptide 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%)
Ejection fraction decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrocardiogram QT prolonged	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrocardiogram ST segment depression	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fibrin D dimer 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%)
Gamma-glutamyltransferase increased	2 (40.00%)	1 (12.50%)	1 (20.00%)	1 (25.00%)	3 (37.50%)	1 (100.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	1 (11.11%)

International normalised ratio increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lipase increased	0 (0.00%)	2 (25.00%)	1 (20.00%)	0 (0.00%)	3 (37.50%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphocyte count decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00%)	1 (11.11%)	1 (100.00%)	1 (16.67%)	0 (0.00%)
Neutrophil count decreased	1 (20.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	4 (50.00%)	1 (100.00%)	0 (0.00%)	2 (50.00%)	3 (33.33%)	0 (0.00%)	3 (50.00%)	1 (11.11%)
N-terminal prohormone brain natriuretic peptide increased	0 (0.00%)	1 (12.50%)	2 (40.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	1 (100.00%)	0 (0.00%)	3 (33.33%)
Nutritional condition abnormal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Occult blood 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%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Platelet count decreased	3 (60.00%)	3 (37.50%)	3 (60.00%)	1 (25.00%)	5 (62.50%)	1 (100.00%)	1 (20.00%)	3 (75.00%)	6 (66.67%)	1 (100.00%)	4 (66.67%)	2 (22.22%)
SARS-CoV-2 test negative	0 (0.00%)	1 (12.50%)	2 (40.00%)	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%)
Thyroxine free increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Thyroxine 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%)
Troponin I increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Troponin increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Troponin T 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%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Weight increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
White blood cell count decreased	2 (40.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	4 (50.00%)	1 (100.00%)	0 (0.00%)	3 (75.00%)	2 (22.22%)	0 (0.00%)	2 (33.33%)	0 (0.00%)
White blood cells urine positive	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders												
Decreased appetite	1 (20.00%)	0 (0.00%)	2 (40.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	1 (16.67%)	3 (33.33%)
Dehydration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Electrolyte imbalance	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gout	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hypercalcaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperglycaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperkalaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperphosphataemia	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertriglyceridaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperuricaemia	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%)
Hypoalbuminaemia	0 (0.00%)	1 (12.50%)	1 (20.00%)	1 (25.00%)	1 (12.50%)	1 (100.00%)	0 (0.00%)	2 (50.00%)	2 (22.22%)	0 (0.00%)	4 (66.67%)	0 (0.00%)
Hypocalcaemia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypokalaemia	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	3 (33.33%)
Hypomagnesaemia	0 (0.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	1 (11.11%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	1 (16.67%)	0 (0.00%)
Hypophosphataemia	1 (20.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Hypoproteinaemia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iron deficiency	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolic acidosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and												

connective tissue disorders												
Arthralgia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Arthritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Back pain	1 (20.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	1 (16.67%)	2 (22.22%)
Bursitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Joint stiffness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Limb discomfort	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Muscular weakness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal chest pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	0 (0.00%)	1 (12.50%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Myositis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Osteonecrosis of jaw	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Shoulder girdle 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%)
Synovitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Trismus	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)												
Tumour associated fever	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (16.67%)	0 (0.00%)
Tumour 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%)	0 (0.00%)
Tumour pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (16.67%)	0 (0.00%)
Nervous system disorders												
Akathisia	0 (0.00%)	0 (0.00%)	0 (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%)
Aphasia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dizziness	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysarthria	0 (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%)
Dysdiadochokinesis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysgeusia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (16.67%)	1 (11.11%)
Headache	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)

Lethargy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Medullary compression syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neuropathy peripheral	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Paraesthesia	0 (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%)
Peripheral sensory neuropathy	0 (0.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Product issues												
Device dislocation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders												
Anxiety	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Confusional state	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Insomnia	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	1 (11.11%)
Renal and urinary disorders												
Choluria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Micturition frequency decreased	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pollakiuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal failure	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary incontinence	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders												
Benign prostatic hyperplasia	0 (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%)
Dysmenorrhoea	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%)
Perineal 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%)
Scrotal oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders												
Aphonia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Aspiration	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Bronchial obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (50.00%)	2 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	1 (16.67%)	1 (11.11%)
Dry throat	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysphonia	0 (0.00%)	1 (12.50%)	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%)
Dyspnoea	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (33.33%)	1 (100.00%)	0 (0.00%)	2 (22.22%)
Dyspnoea exertional	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Epistaxis	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%)
Haemoptysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
Hiccups	0 (0.00%)	0 (0.00%)	0 (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%)
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%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Laryngeal oedema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Lung consolidation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
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%)	1 (11.11%)
Nasal inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Pharyngeal inflammation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleural effusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	2 (22.22%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pleurisy	0 (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%)
Pneumonitis	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (100.00%)	0 (0.00%)	0 (0.00%)
Pneumothorax	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Productive cough	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	1 (100.00%)	0 (0.00%)	1 (11.11%)
Pulmonary embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinorrhoea	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders												
Alopecia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
Dermatitis	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%)
Dermatitis acneiform	0 (0.00%)	1 (12.50%)	1 (20.00%)	0 (0.00%)	1 (12.50%)	1 (100.00%)	0 (0.00%)	0 (0.00%)	3 (33.33%)	0 (0.00%)	0 (0.00%)	1 (11.11%)
Dry skin	1 (20.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	1 (100.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (22.22%)
Eczema	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Night sweats	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Palmar-plantar erythrodysaesthesia syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (11.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Petechiae	0 (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%)
Pruritus	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (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%)
Rash	1 (20.00%)	0 (0.00%)	1 (20.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	1 (20.00%)	1 (25.00%)	0 (0.00%)	0 (0.00%)	2 (33.33%)	0 (0.00%)
Rash macular	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash maculo-papular	1 (20.00%)	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%)
Rash pruritic	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (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%)
Skin exfoliation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin lesion	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin ulcer	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Umbilical haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders												
Embolism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hypertension	1 (20.00 %)	0 (0.00%)	0 (0.00%)	1 (25.00 %)	1 (12.50 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypotension	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Jugular vein thrombosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (20.00 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphoedema	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%)
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%)	0 (0.00%)	1 (11.11 %)

Conclusion:

- TNO155 in combination with spartalizumab and TNO155 in combination with ribociclib appeared well-tolerated at the recommended doses. The AEs are manageable with concomitant treatment and/or dose modifications. Safety profiles of the combinations were consistent with those observed with each single agent. No new safety signals were identified.
- Limited efficacy was observed for both the combination regimens (spartalizumab and ribociclib) in heavily pre-treated patients with advanced malignancy.
- This study was terminated early due to business reasons and not due to any safety concerns.

Date of Clinical Trial Report

10-Oct-2024