Clinical trial results:
Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Multiple Dose Regimens of MT-3724 for the Treatment of Patients with Relapsed non-Hodgkin's B-Cell Lymphoma and B-Cell Chronic Lymphocytic Leukemia (title of protocol for Part 1 and 2); Safety, Pharmacodynamics and Efficacy of MT-3724 for the Treatment of Patients with Relapsed or Refractory DLBCL (Part 3)

Summary

EudraCT number	2019-001073-86
Trial protocol	ES PL GB
Global end of trial date	19 March 2021
Results information	
Result version number	v1 (current)
This version publication date	01 November 2022
First version publication date	01 November 2022
Summary attachment (see zip file)	MT-3724-NHL_001 FDA Premature Closure of Study (MT-3724-NHL_001 FDA Premature Closure of Study_Redacted.pdf) MT-3724-NHL_001 Abbreviated Study Report (MT-3724-NHL_001 Abbreviated Study Report - 16 November 2021_Redacted.pdf) MT-3724-NHL_001 Study Report Synopsis - 22 January 2021 (MT-3724-NHL_001 Study Report Synopsis - 22 January 2021.pdf)

Trial information

Trial identification	
Sponsor protocol code	200MT-3724_NHL_0010
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02361346
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 121918

Notes:

Sponsors	
Sponsor organisation name	Molecular Templates, Inc.
Sponsor organisation address	9301 Amberglen Blvd., Suite 100, Austin, TX, United States, 78729
Public contact	Corporate Headquarters, Molecular Templates, Inc., info@MTEM.com
Scientific contact	Corporate Headquarters, Molecular Templates, Inc., info@MTEM.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 October 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2019
Global end of trial reached?	Yes
Global end of trial date	19 March 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives in Part 1 of the study were to:
• Define the maximum tolerated dose (MTD) of a single cycle of MT-3724 given on Days 1, 3, 5, 8, 10 and 12 at which there are negligible side effects and/or at which maximum pharmacokinetic (PK)/pharmacodynamic (PD) parameter changes are observed.
• Determine PK and PD profiles of MT-3724 in escalating dose cohorts.

In Part 2 of the study, up to 40 additional subjects with relapsed/refractory DLBCL were to be treated with MTD of MT-3724 determined in Part 1 in the MTD expansion cohort. The primary objectives in Part 2 were to:
• Identify the frequency and nature of clinical and laboratory adverse events (AEs), both reported and observed, as a measure of safety and tolerability over repeated cycles of MT-3724 at the MTD.
• Define the PK and PD profiles of MT-3724 at the MTD in this subpopulation.

Protection of trial subjects:

The study was conducted in full compliance with the principles of the "Declaration of Helsinki" (as amended in Tokyo, Venice, Hong Kong, and South Africa), International Council on Harmonisation (ICH) guidelines, and all of the applicable United States (US) Code of Federal Regulations (CFR), 21 CFR Part 50 & 312.

Before undertaking any study-related procedures, the purpose and nature of the study, as well as possible adverse effects, were explained to subjects in understandable terms and written informed consent was obtained from each individual. Each informed consent was to be appropriately signed and dated by the subject and the person obtaining consent.

An independent Data Monitoring Committee (DMC) was established to protect the safety of participants and assure the integrity of the study. The DMC Chair (or designee) reviewed all available safety data for all enrolled subjects on a weekly basis and reviewed causally related severe and/or serious AEs, AESI, or other identified safety trends on a monthly basis. Full DMC meetings were convened as needed. The full DMC met at each end-of-cohort and upon completion/termination of the study to review safety data. The DMC made the recommendation in Part 2 of the study to adjust the MTD from 75 µg/kg to 50 µg/kg/dose with a maximum of 6000 µg/dose based on 2 cases of Grade 2 capillary leak syndrome.

Background therapy:

None.

Evidence for comparator:

None.

Actual start date of recruitment	24 February 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	18 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Georgia: 2
Country: Number of subjects enrolled	Moldova, Republic of: 1
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	27
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Conducted in the United States (5 sites), Moldova (1 site), and Georgia (1 site).

Part 1: first subject enrolled 24 Feb 2015; last subject completed 29 Nov 2016.
Part 2: first subject enrolled 09 Oct 2017; last subject completed 11 Oct 2019.

Pre-assignment

Screening details:

A total of 27 subjects were enrolled and treated at 7 sites in Parts 1 and 2 (1 site did not enroll any subjects). 18 subjects were screen failures due to: inclusion/exclusion criteria not met (17) and consent withdrawn (1).

Period 1

Period 1 title	Part 1 and Part 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 (MT-3724 5 µg/kg)

Arm description:

Part 1: MT-3724 5 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Arm title	Cohort 2 (MT-3724 10 µg/kg)

Arm description:

Part 1: MT-3724 10 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Arm title	Cohort 3 (MT-3724 20 µg/kg)

Arm description:

Part 1: MT-3724 20 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Arm title	Cohort 4 (MT-3724 50 µg/kg)

Arm description:

Part 1: MT-3724 50 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Arm title	Cohort 5 (MT-3724 100 µg/kg)

Arm description:

Part 1: MT-3724 100 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Arm title	Cohort 6 (MT-3724 75 µg/kg)

Arm description:

Part 1: MT-3724 75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The planned dose for cohort 6 was 150 µg/kg. As the maximum tolerated dose (MTD) was exceeded in Cohort 5, an additional dose cohort of 75 µg/kg/dose was added to more narrowly identify the MTD (Cohort 6).

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Arm title	Cohort 7 (MT-3724 50/75 µg/kg)

Arm description:

Part 2: MT-3724 50/75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The first 3 of 6 subjects enrolled in Cohort 7 were treated at 75 µg/kg/dose. The last 3 of 6 subjects were treated with the adjusted MTD (50 µg/kg/dose) following the emergence of Grade 2 capillary leak syndrome (CLS) in 2 subjects in Cohort 7 treated with 75 µg/kg/dose.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1

tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Arm type	Experimental
Investigational medicinal product name	MT-3724
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vial containing 2.0 ml of MT-3724 (0.5 mg/ml) diluted in 5% dextrose in water or normal saline for IV infusion. For Part 1, the infusion time was 2 to 4 hours and for Part 2 the infusion time was 2 hours (± 15 minutes). Subjects received doses of MT-3724 on Days 1, 3, 5, 8, 10, and 12 (within protocol specified time windows).

Number of subjects in period 1	Cohort 1 (MT-3724 5 µg/kg)	Cohort 2 (MT-3724 10 µg/kg)	Cohort 3 (MT-3724 20 µg/kg)
Started	3	3	3
Completed	1	2	0
Not completed	2	1	3
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Disease progression	2	1	3
Adverse event, non-fatal	-	-	-

Number of subjects in period 1	Cohort 4 (MT-3724 50 µg/kg)	Cohort 5 (MT-3724 100 µg/kg)	Cohort 6 (MT-3724 75 µg/kg)
Started	4	2	6
Completed	0	0	1
Not completed	4	2	5
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Disease progression	1	-	4
Adverse event, non-fatal	2	2	1

Number of subjects in period 1	Cohort 7 (MT-3724 50/75 µg/kg)
Started	6
Completed	1
Not completed	5
Adverse event, serious fatal	-
Consent withdrawn by subject	1
Physician decision	1
Disease progression	3
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 (MT-3724 5 µg/kg)

Reporting group description:

Part 1: MT-3724 5 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 2 (MT-3724 10 µg/kg)

Reporting group description:

Part 1: MT-3724 10 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 3 (MT-3724 20 µg/kg)

Reporting group description:

Part 1: MT-3724 20 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 4 (MT-3724 50 µg/kg)

Reporting group description:

Part 1: MT-3724 50 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.

Reporting group title	Cohort 5 (MT-3724 100 µg/kg)

Reporting group description:

Part 1: MT-3724 100 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 6 (MT-3724 75 µg/kg)

Reporting group description:

Part 1: MT-3724 75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The planned dose for cohort 6 was 150 µg/kg. As the maximum tolerated dose (MTD) was exceeded in Cohort 5, an additional dose cohort of 75 µg/kg/dose was added to more narrowly identify the MTD (Cohort 6).

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 7 (MT-3724 50/75 µg/kg)

Reporting group description:

Part 2: MT-3724 50/75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The first 3 of 6 subjects enrolled in Cohort 7 were treated at 75 µg/kg/dose. The last 3 of 6 subjects were treated with the adjusted MTD (50 µg/kg/dose) following the emergence of Grade 2 capillary leak syndrome (CLS) in 2 subjects in Cohort 7 treated with 75 µg/kg/dose.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group values	Cohort 1 (MT-3724 5 µg/kg)	Cohort 2 (MT-3724 10 µg/kg)	Cohort 3 (MT-3724 20 µg/kg)
Number of subjects	3	3	3
Age categorical Units: Subjects			
Age continuous			
Demographic and baseline characteristics were generally well matched between the cohorts, and no notable differences in age, sex, race, ethnicity, and medical/disease history were observed. Overall, the mean (SD) age was 64.6 (10.50) years (Parts 1 and 2) and 64.0 (x) years (Part 3).			
Units: years			
arithmetic mean	73.3	70.7	64.3
standard deviation	± 6.43	± 8.74	± 14.01
Gender categorical			
The majority of subjects were female (63%) in Parts 1 and 2. The majority of subjects were male (72.7%) in Part 3.			
Units: Subjects			
Female	0	2	2
Male	3	1	1
Race			
The majority of subjects were White (85.2%) in Parts 1 and 2. All subjects were White (100%) in Part 3.			
Units: Subjects			
White	2	3	3
Black	0	0	0
Asian	1	0	0
Other	0	0	0
Ethnicity			

The majority of subjects were of Non-Hispanic origin (88.9% in Parts 1 and 2; 90.9% in Part 3).			
Units: Subjects			
Hispanic	0	0	0
Non-Hispanic	3	3	3
Unknown	0	0	0
Height			
The subjects' height was measured at Screening. The overall mean (SD) height was 164.00 (8.33) cm (Parts 1 and 2) and 173.1 cm (Part 3).			
Units: cm			
arithmetic mean	165.17	164.73	172.33
standard deviation	± 8.31	± 3.95	± 9.07
Weight			
Body weight measured before the start of treatment on C1D1 was used to calculate the MT-3724 dose in all subsequent cycles. The dose was re-calculated when the body weight changed by >10% from the baseline value; or according to institutional policies should they require adjustment for any change in body weight. The overall mean (SD) weight was 80.61 (22.17) kg.			
Units: kg			
arithmetic mean	74.83	81.20	65.70
standard deviation	± 17.79	± 14.37	± 11.14

Reporting group values	Cohort 4 (MT-3724 50 µg/kg)	Cohort 5 (MT-3724 100 µg/kg)	Cohort 6 (MT-3724 75 µg/kg)
Number of subjects	4	2	6
Age categorical			
Units: Subjects			
Age continuous			
Demographic and baseline characteristics were generally well matched between the cohorts, and no notable differences in age, sex, race, ethnicity, and medical/disease history were observed. Overall, the mean (SD) age was 64.6 (10.50) years (Parts 1 and 2) and 64.0 (x) years (Part 3).			
Units: years			
arithmetic mean	57.8	65.0	67.2
standard deviation	± 16.66	± 4.24	± 4.40
Gender categorical			
The majority of subjects were female (63%) in Parts 1 and 2. The majority of subjects were male (72.7%) in Part 3.			
Units: Subjects			
Female	3	1	4
Male	1	1	2
Race			
The majority of subjects were White (85.2%) in Parts 1 and 2. All subjects were White (100%) in Part 3.			
Units: Subjects			
White	2	2	5
Black	0	0	0
Asian	0	0	1
Other	2	0	0
Ethnicity			
The majority of subjects were of Non-Hispanic origin (88.9% in Parts 1 and 2; 90.9% in Part 3).			
Units: Subjects			
Hispanic	2	0	0
Non-Hispanic	2	2	6
Unknown	0	0	0

Height			
The subjects' height was measured at Screening. The overall mean (SD) height was 164.00 (8.33) cm (Parts 1 and 2) and 173.1 cm (Part 3).			
Units: cm			
arithmetic mean	157.20	168.10	162.73
standard deviation	± 6.39	± 2.97	± 6.32
Weight			
Body weight measured before the start of treatment on C1D1 was used to calculate the MT-3724 dose in all subsequent cycles. The dose was re-calculated when the body weight changed by >10% from the baseline value; or according to institutional policies should they require adjustment for any change in body weight. The overall mean (SD) weight was 80.61 (22.17) kg.			
Units: kg			
arithmetic mean	70.58	96.55	72.82
standard deviation	± 6.99	± 17.04	± 20.36

Reporting group values	Cohort 7 (MT-3724 50/75 µg/kg)	Total	
Number of subjects	6	27	
Age categorical			
Units: Subjects			
Age continuous			
Demographic and baseline characteristics were generally well matched between the cohorts, and no notable differences in age, sex, race, ethnicity, and medical/disease history were observed. Overall, the mean (SD) age was 64.6 (10.50) years (Parts 1 and 2) and 64.0 (x) years (Part 3).			
Units: years			
arithmetic mean	59.3		
standard deviation	± 10.58	-	
Gender categorical			
The majority of subjects were female (63%) in Parts 1 and 2. The majority of subjects were male (72.7%) in Part 3.			
Units: Subjects			
Female	5	17	
Male	1	10	
Race			
The majority of subjects were White (85.2%) in Parts 1 and 2. All subjects were White (100%) in Part 3.			
Units: Subjects			
White	6	23	
Black	0	0	
Asian	0	2	
Other	0	2	
Ethnicity			
The majority of subjects were of Non-Hispanic origin (88.9% in Parts 1 and 2; 90.9% in Part 3).			
Units: Subjects			
Hispanic	0	2	
Non-Hispanic	5	24	
Unknown	1	1	
Height			
The subjects' height was measured at Screening. The overall mean (SD) height was 164.00 (8.33) cm (Parts 1 and 2) and 173.1 cm (Part 3).			
Units: cm			
arithmetic mean	163.30		
standard deviation	± 11.77	-	
Weight			

Body weight measured before the start of treatment on C1D1 was used to calculate the MT-3724 dose in all subsequent cycles. The dose was re-calculated when the body weight changed by >10% from the baseline value; or according to institutional policies should they require adjustment for any change in body weight. The overall mean (SD) weight was 80.61 (22.17) kg.			
Units: kg			
arithmetic mean	99.83		
standard deviation	± 30.73	-	

End points reporting groups

Reporting group title	Cohort 1 (MT-3724 5 µg/kg)

Reporting group description:

Part 1: MT-3724 5 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 2 (MT-3724 10 µg/kg)

Reporting group description:

Part 1: MT-3724 10 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 3 (MT-3724 20 µg/kg)

Reporting group description:

Part 1: MT-3724 20 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 4 (MT-3724 50 µg/kg)

Reporting group description:

Part 1: MT-3724 50 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.

Reporting group title	Cohort 5 (MT-3724 100 µg/kg)

Reporting group description:

Part 1: MT-3724 100 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 6 (MT-3724 75 µg/kg)

Reporting group description:

Part 1: MT-3724 75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The planned dose for cohort 6 was 150 µg/kg. As the maximum tolerated dose (MTD) was exceeded in Cohort 5, an additional dose cohort of 75 µg/kg/dose was added to more narrowly identify the MTD (Cohort 6).

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Reporting group title	Cohort 7 (MT-3724 50/75 µg/kg)

Reporting group description:

Part 2: MT-3724 50/75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The first 3 of 6 subjects enrolled in Cohort 7 were treated at 75 µg/kg/dose. The last 3 of 6 subjects were treated with the adjusted MTD (50 µg/kg/dose) following the emergence of Grade 2 capillary leak syndrome (CLS) in 2 subjects in Cohort 7 treated with 75 µg/kg/dose.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for demographic/baseline characteristics and safety analyses.

The Full Analysis set (FAS) population included all subjects from the Safety Set (SS) who had a least 1 tumor re-evaluation performed (scheduled or unscheduled). The FAS was the primary population for all exploratory efficacy analyses.

Subject analysis set title	Combined 50 µg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Combined (50 µg/kg/dose) analysis set includes all subjects with a starting dose of 50 µg/kg in Part 1 or Part 2.

Subject analysis set title	All Subjects
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	5 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	10 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	20 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	37.5 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	50 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	75 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Subject analysis set title	100 µg/kg (PAS)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic Analysis Set (PAS) included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Primary: Adverse Events (Safety Set)

End point title	Adverse Events (Safety Set)[1]

End point description:

Safety assessments of all AEs included DLTs. Cumulative AE data were reviewed periodically by the DMC as well as ad hoc review of SAEs and/or severe AEs as they were reported. AEs were assessed using the CTCAE, version 4.03.

Parts 1 and 2: All 27 subjects had at least 1 TEAE and 26 subjects (96.3%) had at least 1 treatment-related TEAE. 14 subjects (51.9%) had at least 1 serious TEAE, and 6 subjects (22.2%) had at least 1 treatment-related serious TEAE. There were no differences in incidences of the most common TEAEs between the cohorts.

There was 1 subject (Subject 01005 in Cohort 4) with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.

End point type	Primary

End point timeframe:

Safety was monitored throughout the study.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was primarily descriptive in nature; therefore, there were no formal statistical hypothesis tests were planned.

End point values	Cohort 1 (MT-3724 5 µg/kg)	Cohort 2 (MT-3724 10 µg/kg)	Cohort 3 (MT-3724 20 µg/kg)	Cohort 4 (MT-3724 50 µg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[2]	3	3[3]	4[4]
Units: subjects				
At least 1 TEAE	3	3	3	4
At least 1 treatment-related (TR) TEAE	3	3	2	4
At least 1 TEAE with severity ≥Grade 3	3	0	2	4
At least 1 TR TEAE with severity ≥Grade 3	1	0	0	2
At least 1 non-serious TEAE	3	3	3	4
At least 1 non-serious TR TEAE	3	3	2	4
At least 1 serious TEAE	1	0	2	4
At least 1 serious TR TEAE	0	0	0	1
At least 1 TEAE leading to early study withdrawal	0	0	0	2
At least 1 DLT	0	0	0	0

At least 1 TEAE leading to death	0	0	0	1
A TR TEAE leading to death	0	0	0	0

Notes:

[2] - TR TEAE ≥ Grade 3 = 33.3%; serious TEAE = 33.3%

[3] - TR TEAE = 66.7%; TEAE ≥ Grade 3 = 66.7%; non-serious TR TEAE = 66.7%; serious TEAE = 66.7%

[4] - TR TEAE ≥Gr 3 =50%; serious TR TEAE =25%; TEAE early withdrawal =50%;TEAE leading to death =25%.

End point values	Cohort 5 (MT-3724 100 µg/kg)	Cohort 6 (MT-3724 75 µg/kg)	Cohort 7 (MT-3724 50/75 µg/kg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	6[5]	6[6]	
Units: subjects				
At least 1 TEAE	2	6	6	
At least 1 treatment-related (TR) TEAE	2	6	6	
At least 1 TEAE with severity ≥Grade 3	2	3	6	
At least 1 TR TEAE with severity ≥Grade 3	2	2	6	
At least 1 non-serious TEAE	2	6	6	
At least 1 non-serious TR TEAE	2	6	6	
At least 1 serious TEAE	2	3	2	
At least 1 serious TR TEAE	2	2	1	
At least 1 TEAE leading to early study withdrawal	2	1	0	
At least 1 DLT	2	0	0	
At least 1 TEAE leading to death	0	0	0	
A TR TEAE leading to death	0	0	0	

Notes:

[5] - TEAE ≥Gr3 =50%; TR TEAE ≥Gr3 = 33.3%; serious TEAE=50%; serious TR TEAE =33.3%; TEAE early w/d 16.7%

[6] - Serious TEAE = 33.3%; serious TR TEAE = 16.7%

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Maximum Observed Serum Concentration (Cmax) (PAS)

End point title	Maximum Observed Serum Concentration (Cmax) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Overall, Day 1 maximum observed serum concentration (Cmax) increased with increasing dose level but were variable, with geometric coefficient of variation (CV%) (where calculable) ranging from 42.7% to 77.8%.

'99999' indicates the value was not reported (NR) or not calculated for the timepoint.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[7]	3	3	7
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)	57.5 (± 99999)	70.4 (± 61.9)	132 (± 46.6)	445 (± 42.7)

Notes:

[7] - Geometric coefficient of variation was not calculated.

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2[8]		
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)	486 (± 77.8)	828 (± 99999)		

Notes:

[8] - Geometric coefficient of variation was not calculated.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to Maximum Plasma Concentration (Tmax) (PAS)

End point title	Time to Maximum Plasma Concentration (Tmax) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

Time to maximum plasma concentration (Tmax) was similar across dose levels with medians ranging from 1.85 to 3.29 hours post-start of infusion, which was largely due to variability in infusion duration.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	3	3	7
Units: hour				
median (full range (min-max))	2.10 (2.10 to 2.10)	2.08 (1.97 to 3.00)	2.08 (2.08 to 2.08)	2.32 (2.08 to 2.58)

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2		
Units: hour				
median (full range (min-max))	1.85 (1.70 to 4.42)	3.29 (2.50 to 4.08)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to last measurable plasma concentration (Tlast) (PAS)

End point title	Time to last measurable plasma concentration (Tlast) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	3	3	7
Units: hour				
median (full range (min-max))	5.00 (5.00 to 5.00)	3.00 (2.82 to 6.00)	5.92 (4.08 to 6.00)	6.00 (5.92 to 6.82)

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2		
Units: hour				
median (full range (min-max))	5.92 (3.00 to 8.00)	7.24 (6.48 to 8.00)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area under concentration-time curve from time 0 to the last quantifiable concentration (AUClast) (PAS)

End point title	Area under concentration-time curve from time 0 to the last quantifiable concentration (AUClast) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

'99999' indicates the value was not reported (NR) or not calculated for the timepoint.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[9]	3	3	7
Units: hour*nanogram/millilitre				
geometric mean (geometric coefficient of variation)	170 (± 99999)	155 (± 155)	333 (± 73.2)	1370 (± 32.1)

Notes:

[9] - Geometric coefficient of variation was not calculated.

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2[10]		
Units: hour*nanogram/millilitre				
geometric mean (geometric coefficient of variation)	1410 (± 102)	2980 (± 99999)		

Notes:

[10] - Geometric coefficient of variation was not calculated.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area Under Concentration-time Curve from Time 0 to 4 hours (AUC0-4) (PAS)

End point title	Area Under Concentration-time Curve from Time 0 to 4 hours (AUC0-4) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

The area under concentration-time curve from time 0 to 4 hours (AUC0-4) increased with increasing dose in an approximately dose-proportional manner from 5 to 100 µg/kg. Compared to Day 1, there were fewer PK samples collected on Days 5 and 12, resulting in fewer evaluable PK profiles.

'99999' indicates the value was not reported (NR) or not calculated for the timepoint.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[11]	1[12]	3	7
Units: h*nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)	140 (± 99999)	365 (± 99999)	278 (± 56.2)	1040 (± 35.1)

Notes:

[11] - Geometric coefficient of variation was not calculated.

[12] - Geometric coefficient of variation was not calculated.

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2[13]		
Units: h*nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)	1060 (± 95.2)	1650 (± 99999)		

Notes:

[13] - Geometric coefficient of variation was not calculated.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area under concentration-time curve from time 0 to infinity (AUCinf) (PAS)

End point title	Area under concentration-time curve from time 0 to infinity (AUCinf) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

'99999' indicates the value was not reported (NR) or not calculated for the timepoint.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[14]	0[15]	3	7
Units: h*nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)	()	()	451 (± 87.5)	1680 (± 28.3)

Notes:

[14] - The AUCinf was not reportable for the 5 and 10 µg/kg cohorts.

[15] - The AUCinf was not reportable for the 5 and 10 µg/kg cohorts.

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2[16]		
Units: h*nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)	1680 (± 114)	3970 (± 99999)		

Notes:

[16] - Geometric coefficient of variation was not calculated.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Half-life (t1/2) (PAS)

End point title	Half-life (t1/2) (PAS)

End point description:

PK serum samples were analyzed for concentrations of free MT-3724. PK analyses were conducted using the PAS, which included all subjects from the SS with sufficient serum concentration data to determine the primary PK parameters.

The t½ was not reportable for the 5 and 10 µg/kg cohorts, but geometric means were similar for the 20 to 100 µg/kg cohorts, ranging from 1.50 to 2.83 hours.

'99999' indicates the value was not reported (NR) or not calculated for the timepoint.

End point type	Other pre-specified

End point timeframe:

Blood samples were collected prior to, during, and at specified times following the MT-3724 infusion for determination of free MT-3724 concentrations in serum (Cycle 1 on Days 1, 3, and 12). Serum PK parameters on Cycle 1 Day 1 are presented.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	50 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[17]	0[18]	3	7
Units: hour				
geometric mean (geometric coefficient of variation)	()	()	2.07 (± 58.6)	1.92 (± 32.1)

Notes:

[17] - The t½ was not reportable for the 5 and 10 µg/kg cohorts.

[18] - The t½ was not reportable for the 5 and 10 µg/kg cohorts.

End point values	75 µg/kg (PAS)	100 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	2[19]		
Units: hour				
geometric mean (geometric coefficient of variation)	1.50 (± 59.0)	2.78 (± 99999)		

Notes:

[19] - Geometric coefficient of variation was not calculated.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: CD19+ Change (%) (PAS)

End point title	CD19+ Change (%) (PAS)

End point description:

The number of subjects in each dose group with CD19+ flow cytometry data was generally low, leading to high variability and mean changes in CD19+ values that were sensitive to a single subject’s data.

Generally, mean percentage of CD19+ cells from the peripheral blood decreased after treatment. On Cycle 1 Day 23 and Cycle 2 Day 1, 7 of 9 subjects demonstrated decreased percentage of CD19+ cells compared to baseline. At the End of Study, 9 of 10 subjects demonstrated decreased CD19+ compared to baseline.

'99999' indicates the value was not reported (NR) or not calculated (<3 evaluable subjects) for the timepoint.

End point type	Other pre-specified

End point timeframe:

Serial blood samples for PD assessment were collected at Screening, Cycle 1 Day 8, Cycle 1 Day 23, Cycle 3 Day 1, Cycle 5 Day 1, and EOT. Unscheduled assessments could be performed at any time at the investigator’s discretion.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	37.5 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	2	1	1
Units: percent				
geometric mean (geometric coefficient of variation)				
Screening	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1 Day 8	0 (± 99999)	34.2 (± 99999)	0 (± 99999)	167 (± 99999)
Cycle 1 Day 23	25.4 (± 99999)	-60.2 (± 99999)	-46.3 (± 99999)	99999 (± 99999)
Cycle 3 Day 1	-41.2 (± 99999)	-50.9 (± 99999)	-75.4 (± 99999)	99999 (± 99999)
Cycle 5 Day 1	15.8 (± 99999)	-35.4 (± 99999)	-78.3 (± 99999)	99999 (± 99999)

End of Study	-30.7 (± 99999)	-23.7 (± 99999)	-79.9 (± 99999)	-63.0 (± 99999)

End point values	50 µg/kg (PAS)	75 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4[20]	1		
Units: percent				
geometric mean (geometric coefficient of variation)				
Screening	99999 (± 99999)	99999 (± 99999)		
Cycle 1 Day 8	-49.1 (± -87.8)	-57.4 (± 99999)		
Cycle 1 Day 23	99999 (± 99999)	-77.4 (± 99999)		
Cycle 3 Day 1	-48.2 (± -54.1)	-88.5 (± 99999)		
Cycle 5 Day 1	-72.1 (± 99999)	-86.8 (± 99999)		
End of Study	-63.3 (± -45.9)	-85.1 (± 99999)		

Notes:

[20] - Sample size: Screening: NR; C1D8: n=3; C1D23: NR; C3D1: n=3; C5D1: n=2; EOS: n=4

Statistical analyses

No statistical analyses for this end point

Other pre-specified: CD19+ Absolute (PAS)

End point title	CD19+ Absolute (PAS)

End point description:

Flow cytometry: Individual lymphocyte subset analyses were presented graphically by dose and time based on 2 types of cell quantification; percent of baseline and absolute cell count.

At the EOT, 9 of 10 subjects demonstrated decreased CD19+ compared to baseline. Due to high variability in the data, small sample size, and inconsistent sampling, PK-PD relationships were difficult to discern.

'99999' indicates the value was not reported (NR) or not calculated (<3 evaluable subjects) for the timepoint.

End point type	Other pre-specified

End point timeframe:

Serial blood samples for PD assessment were collected at Screening, Cycle 1 Day 8, Cycle 1 Day 23, Cycle 3 Day 1, Cycle 5 Day 1, and EOT. Unscheduled assessments could be performed at any time at the investigator’s discretion.

End point values	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)	37.5 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1	2	1	1
Units: cells/microlitre				
geometric mean (geometric coefficient of variation)				
Screening	99999 (± 99999)	286 (± 99999)	99999 (± 99999)	99999 (± 99999)
Cycle 1 Day 8	114 (± 99999)	325 (± 99999)	244 (± 99999)	72.0 (± 99999)
Cycle 1 Day 23	143 (± 99999)	104 (± 99999)	131 (± 99999)	99999 (± 99999)
Cycle 3 Day 1	67.0 (± 99999)	134 (± 99999)	60.0 (± 99999)	99999 (± 99999)
Cycle 5 Day 1	132 (± 99999)	180 (± 99999)	53.0 (± 99999)	99999 (± 99999)
End of Study	79.0 (± 99999)	184 (± 99999)	49.0 (± 99999)	10.0 (± 99999)

End point values	50 µg/kg (PAS)	75 µg/kg (PAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4[21]	3[22]		
Units: cells/microlitre				
geometric mean (geometric coefficient of variation)				
Screening	84.0 (± 133)	1180 (± 172)		
Cycle 1 Day 8	57.7 (± 158)	126 (± 99999)		
Cycle 1 Day 23	99999 (± 99999)	67.0 (± 99999)		
Cycle 3 Day 1	1170 (± 168)	34.0 (± 99999)		
Cycle 5 Day 1	26.0 (± 99999)	39.0 (± 99999)		
End of Study	340 (± 177)	44.0 (± 99999)		

Notes:

[21] - Sample size: Screening: n=3; C1D8: n=3; C1D23: NR; C3D1: n=3; C5D1: n=2; EOS: n=4

[22] - Sample size: Screening: n=3; C1D8: n=1; C1D23: n=1; C3D1: n=1; C5D1: n=1; EOS: n=1

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Anti-Drug Antibody Incidence by Actual Dose

End point title	Anti-Drug Antibody Incidence by Actual Dose

End point description:

Anti-drug antibodies (ADAs) in serum of subjects with NHL or CLL at baseline and following exposure to MT-3724 were assessed.

Overall, the presence of ADAs increased with the duration of treatment, and there was no apparent relationship between MT-3724 dose level and ADA incidence. Safety events observed in the trial did not seem to correlate with presence of ADAs. Also based on data available clinical response was not observed to be confounded by presence of ADAs.

End point type	Other pre-specified

End point timeframe:

During Parts 1 and 2, blood samples for immunogenicity assessments of ADAs were collected at Screening, Day 23, pre-dose for Cycles 2 through 5, and EOT. Additional samples were taken if clinically indicated.

End point values	All Subjects	5 µg/kg (PAS)	10 µg/kg (PAS)	20 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	27[23]	3[24]	3[25]	3[26]
Units: subjects				
Screening	5	2	0	0
Cycle 1 Day 23	6	0	3	1
Cycle 2 Day 1	11	0	3	1
Cycle 3 Day 1	6	0	2	1
Cycle 4 Day 1	7	1	2	1
Cycle 5 Day 1	6	1	2	1
End of Study	13	2	2	1

Notes:

[23] - Sample size: Screening: n=27; C1D23: n=15; C2D1: n=20; C3D1: n=8; C4D1: n=8; C5D1: n=7; EOS: n=20

[24] - Sample size: Screening: n=3; C1D23: n=1; C2D1: n=1; C3D1: n=1; C4D1: n=1; C5D1: n=1; EOS: n=3

[25] - Sample size: Screening: n=3; C1D23: n=3; C2D1: n=3; C3D1: n=2; C4D1: n=2; C5D1: n=2; EOS: n=2

[26] - Sample size: Screening: n=3; C1D23: n=2; C2D1: n=2; C3D1: n=1; C4D1: n=1; C5D1: n=1; EOS: n=2

End point values	37.5 µg/kg (PAS)	50 µg/kg (PAS)	75 µg/kg (PAS)	100 µg/kg (PAS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[27]	7[28]	9[29]	2[30]
Units: subjects				
Screening	0	2	0	1
Cycle 1 Day 23	0	1	1	0
Cycle 2 Day 1	1	4	2	0
Cycle 3 Day 1	0	2	1	0
Cycle 4 Day 1	0	2	1	0
Cycle 5 Day 1	0	1	1	0
End of Study	1	4	3	0

Notes:

[27] - Sample size: Screening: n=0; C1D23: n=0; C2D1: n=1; C3D1: n=0; C4D1: n=0; C5D1: n=0; EOS: n=1

[28] - Sample size: Screening: n=7; C1D23: n=3; C2D1: n=6; C3D1: n=3; C4D1: n=3; C5D1: n=2; EOS: n=6

[29] - Sample size: Screening: n=9; C1D23: n=5; C2D1: n=7; C3D1: n=1; C4D1: n=1; C5D1: n=1; EOS: n=5

[30] - Sample size: Screening: n=2; C1D23: n=1; C2D1: n=0; C3D1: n=0; C4D1: n=0; C5D1: n=0; EOS: n=1

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Best Overall Response (FAS)

End point title	Best Overall Response (FAS)

End point description:

The MTD was identified as 50 µg/kg/dose. The first 2 subjects in Part 1 treated at 100 µg/kg had 1 dose limiting toxicity (DLT) each (Grade 3 pneumonia and Grade 2 ileus). Therefore, 75 µg/kg was initially

declared to be the MTD. In Part 2 of the study, 2 of 3 subjects treated at 75 µg/kg had DLTs of Grade 2 CLS. Because these events led to dose reduction in both subjects, MTD was adjusted to 50 µg/kg.

Best overall response (BOR) at any time during the study, as determined by the Cheson criteria on at least 1 post-baseline tumor assessment. This included complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD).

End point type	Other pre-specified

End point timeframe:

Disease response was assessed following completion of even numbered (e.g., 2, 4) cycles of MT-3724 and at the final safety assessment (optional) following termination of MT-3724 using standard disease response criteria.

End point values	Cohort 1 (MT-3724 5 µg/kg)	Cohort 2 (MT-3724 10 µg/kg)	Cohort 3 (MT-3724 20 µg/kg)	Cohort 4 (MT-3724 50 µg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[31]	3[32]	3[33]	4[34]
Units: subjects				
Complete Remission	0	0	0	0
Unconfirmed/Uncertain Complete Remission	0	0	0	0
Partial Remission	1	0	1	0
Stable Disease	0	2	0	0
Progressive Disease	2	1	2	3
Not Evaluable	0	0	0	0

Notes:

[31] - PR: 33.3%; PD: 66.7%

[32] - SD: 66.7%; PD: 33.3%

[33] - PR: 33.3%; PD: 66.7%

[34] - PD: 100.0%

End point values	Cohort 5 (MT-3724 100 µg/kg)	Cohort 6 (MT-3724 75 µg/kg)	Cohort 7 (MT-3724 50/75 µg/kg)	Combined 50 µg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	2[35]	6[36]	6[37]	6[38]
Units: subjects				
Complete Remission	0	0	2	2
Unconfirmed/Uncertain Complete Remission	0	0	0	0
Partial Remission	0	0	1	0
Stable Disease	1	1	1	0
Progressive Disease	0	3	2	4
Not Evaluable	0	0	0	0

Notes:

[35] - SD: 100.0%

[36] - SD: 25.0%; PD: 75.0%

[37] - CR: 33.3%; PR: 16.7%; SD: 16.7%; PD: 33.3%

[38] - CR: 33.3%; PD: 66.7%

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Objective Response Rate (FAS)

End point title	Objective Response Rate (FAS)

End point description:

The MTD was identified as 50 µg/kg/dose. The first 2 subjects in Part 1 treated at 100 µg/kg had 1 DLT each (Grade 3 pneumonia and Grade 2 ileus). Therefore, 75 µg/kg was initially declared to be the MTD. In Part 2 of the study, 2 of 3 subjects treated at 75 µg/kg had DLTs of Grade 2 CLS. Because these events led to dose reduction in both subjects, MTD was adjusted to 50 µg/kg.

Objective Response Rate (ORR), defined as the proportion of subjects with either CR or PR as determined by the Cheson criteria.

As this was a dose finding study designed to assess the safety and tolerability of MT-3724, all efficacy analyses were exploratory in nature and based on documented tumor responses. Due to the limited treatment period following responses, no interpretation of the results could be made.

End point type	Other pre-specified

End point timeframe:

Disease response was assessed following completion of even numbered (e.g., 2, 4) cycles of MT-3724 and at the final safety assessment (optional) following termination of MT-3724 using standard disease response criteria.

End point values	Cohort 1 (MT-3724 5 µg/kg)	Cohort 2 (MT-3724 10 µg/kg)	Cohort 3 (MT-3724 20 µg/kg)	Cohort 4 (MT-3724 50 µg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[39]	3	3[40]	4
Units: percent				
number (confidence interval 95%)				
Objective Response Rate (ORR)	33.3 (0.8 to 90.6)	0 (0 to 0)	33.3 (0.8 to 90.6)	0 (0 to 0)

Notes:

[39] - ORR: n=1

[40] - ORR: n=1

End point values	Cohort 5 (MT-3724 100 µg/kg)	Cohort 6 (MT-3724 75 µg/kg)	Cohort 7 (MT-3724 50/75 µg/kg)	Combined 50 µg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	2	6	6[41]	6[42]
Units: percent				
number (confidence interval 95%)				
Objective Response Rate (ORR)	0 (0 to 0)	0 (0 to 0)	50.0 (11.8 to 88.2)	33.3 (4.3 to 77.7)

Notes:

[41] - ORR: n=3

[42] - ORR: n=2

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Disease Control Rate (FAS)

End point title	Disease Control Rate (FAS)

End point description:

The MTD was identified as 50 µg/kg/dose. The first 2 subjects in Part 1 treated at 100 µg/kg had 1 DLT each (Grade 3 pneumonia and Grade 2 ileus). Therefore, 75 µg/kg was initially declared to be the MTD. In Part 2 of the study, 2 of 3 subjects treated at 75 µg/kg had DLTs of Grade 2 CLS. Because these events led to dose reduction in both subjects, MTD was adjusted to 50 µg/kg.

Disease control rate (DCR), defined as the proportion of subjects with either CR, PR, or SD as determined by the Cheson criteria.

As this was a dose finding study designed to assess the safety and tolerability of MT-3724, all efficacy analyses were exploratory in nature and based on documented tumor responses. Due to the limited treatment period following responses, no interpretation of the results could be made.

End point type	Other pre-specified

End point timeframe:

Disease response was assessed following completion of even numbered (e.g., 2, 4) cycles of MT-3724 and at the final safety assessment (optional) following termination of MT-3724 using standard disease response criteria.

End point values	Cohort 1 (MT-3724 5 µg/kg)	Cohort 2 (MT-3724 10 µg/kg)	Cohort 3 (MT-3724 20 µg/kg)	Cohort 4 (MT-3724 50 µg/kg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3[43]	3[44]	3[45]	4
Units: percent				
number (confidence interval 95%)				
Disease Control Rate	33.3 (0.8 to 90.6)	66.7 (9.4 to 99.2)	33.3 (0.8 to 90.6)	0 (0 to 0)

Notes:

[43] - DCR: n=1

[44] - DCR: n=2

[45] - DCR: n=3

End point values	Cohort 5 (MT-3724 100 µg/kg)	Cohort 6 (MT-3724 75 µg/kg)	Cohort 7 (MT-3724 50/75 µg/kg)	Combined 50 µg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	2[46]	6[47]	6[48]	6[49]
Units: percent				
number (confidence interval 95%)				
Disease Control Rate	100.0 (2.5 to 100.0)	25.0 (0.6 to 80.6)	66.7 (22.3 to 95.7)	33.3 (4.3 to 77.7)

Notes:

[46] - DCR: n=1

[47] - DCR: n=1

[48] - DCR: n=4

[49] - DCR: n=2

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

AE reporting began on the day of the first dose of study drug after signing informed consent until the STFU Visit or phone call, or until the start of new cancer therapy, whichever occurred first.

Adverse event reporting additional description:

TEAEs were all AEs that started or worsened after the first administration of MT-3724 up until the last study visit.

Safety results are presented for the SS, which included all subjects who received any amount of MT-3724.

If a subject experienced more than 1 event with a given SOC or PT, that subject was counted only once for that SOC or PT.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Cohort 1 (5 µg/kg)

Reporting group description:

Part 1: MT-3724 5 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

Reporting group title	Cohort 2 (10 µg/kg)

Reporting group description:

Part 1: MT-3724 10 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

Reporting group title	Cohort 3 (20 µg/kg)

Reporting group description:

Part 1: MT-3724 20 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

Reporting group title	Cohort 4 (50µg/kg)

Reporting group description:

Part 1: MT-3724 50 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.

Reporting group title	Cohort 5 (100 µg/kg)

Reporting group description:

Part 1: MT-3724 100 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

Reporting group title	Cohort 6 (75 µg/kg)

Reporting group description:

Part 1: MT-3724 75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

Planned dose for cohort 6 was 150 µg/kg. As the MTD was exceeded in Cohort 5, an additional dose cohort of 75 µg/kg/dose was added to more narrowly identify the MTD (Cohort 6).

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

Reporting group title	Cohort 7 (50/75 µg/kg)

Reporting group description:

Part 2: MT-3724 50/75 µg/kg administered as an initial 12-day course followed by at least a 2-week observation period providing a study period of 28 days in total.

The first 3 of 6 subjects enrolled in Cohort 7 were treated at 75 µg/kg/dose. The last 3 of 6 subjects were treated with the adjusted MTD (50 µg/kg/dose) following the emergence of grade 2 CLS in 2 subjects in Cohort 7 treated with 75 µg/kg/dose.

The Safety Set (SS) included all subjects who received any amount of MT-3724. The SS was the primary population for the analysis of safety.

Serious adverse events	Cohort 1 (5 µg/kg)	Cohort 2 (10 µg/kg)	Cohort 3 (20 µg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest	Additional description: There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.		
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure	Additional description: Renal failure acute		
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4 (50µg/kg)	Cohort 5 (100 µg/kg)	Cohort 6 (75 µg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	2 / 2 (100.00%)	3 / 6 (50.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest	Additional description: There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.		

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure	Additional description: Renal failure acute		
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superinfection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 7 (50/75 µg/kg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest	Additional description: There was 1 subject in Cohort 4 with a TEAE (PT: cardiac arrest) leading to death; this TEAE was considered to be unrelated to treatment and secondary to disease progression.		
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Iron deficiency anaemia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Ileus			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure	Additional description: Renal failure acute		
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Superinfection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1 (5 µg/kg)	Cohort 2 (10 µg/kg)	Cohort 3 (20 µg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flushing			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fatigue			

subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	3	1	2
Infusion site irritation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Injection site extravasation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Swelling	Additional description: Local swelling		
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	1
Dysphonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocapnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Laryngeal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dysphoria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Scratch			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood chloride increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactic acid increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Heart rate increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiomyopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myocardial ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Neuropathy peripheral			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Presyncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lymph node pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Ear and labyrinth disorders			
Ear disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Retinal exudates			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			

subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysphagia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Reflux gastritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Vomiting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cold sweat			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Ecchymosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pruritus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Skin exfoliation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Groin pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Pyoderma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoproteinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 4 (50µg/kg)	Cohort 5 (100 µg/kg)	Cohort 6 (75 µg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	2 / 2 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Haematoma			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Chills			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Face oedema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Infusion site irritation			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site extravasation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Swelling	Additional description: Local swelling		
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	4 / 4 (100.00%)	1 / 2 (50.00%)	4 / 6 (66.67%)
occurrences (all)	4	1	4
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	3 / 6 (50.00%)
occurrences (all)	1	1	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dyspnoea			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Dyspnoea exertional			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypocapnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Laryngeal inflammation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	4
Pleural effusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pulmonary hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Throat irritation			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphoria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Scratch			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wound			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood chloride increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood lactic acid increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Heart rate increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cardiomyopathy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myocardial ischaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Dysgeusia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	1 / 6 (16.67%)
occurrences (all)	2	1	1
Leukocytosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymph node pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pancytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear disorder			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Retinal exudates			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	3 / 6 (50.00%)
occurrences (all)	2	1	3
Dyspepsia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Gastric ulcer			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Melaena			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Oral pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Reflux gastritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vomiting			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cold sweat			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Hyperhidrosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Skin exfoliation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Musculoskeletal pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 2 (100.00%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Neck pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Pyoderma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Troponin increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Failure to thrive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Hypoalbuminaemia			

subjects affected / exposed	2 / 4 (50.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 2 (100.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Hypoproteinaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 7 (50/75 µg/kg)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Flushing			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Haematoma			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Lymphoedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Venous thrombosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Face oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Infusion site irritation			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site extravasation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Swelling	Additional description: Local swelling		
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dyspnoea			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Dyspnoea exertional				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Hiccups				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Hypocapnia				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Laryngeal inflammation				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Nasal congestion				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Oropharyngeal pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pleural effusion				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Pneumonitis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pulmonary embolism				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Pulmonary hypertension				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Respiratory tract congestion				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Throat irritation				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysphoria			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Wound			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood chloride increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Blood lactic acid increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Heart rate increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lipase increased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Neutrophil count decreased				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Platelet count decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Weight increased				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	3			
White blood cell count decreased				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cardiomyopathy			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myocardial ischaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Memory impairment			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Paraesthesia			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Presyncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Somnolence subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Leukocytosis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Leukopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Lymph node pain subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Pancytopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0		
Ear and labyrinth disorders Ear disorder			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Retinal exudates			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Retinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ascites			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Dyspepsia			

subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Gastric ulcer				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Haemorrhoids				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Melaena				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Mouth haemorrhage				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Oral pain				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Reflux gastritis				
subjects affected / exposed	0 / 6 (0.00%)			
occurrences (all)	0			
Stomatitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Vomiting				

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Blister			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Cold sweat			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Dermatitis acneiform			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pruritus			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Skin exfoliation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			

subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	3 / 6 (50.00%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Folliculitis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

Pyoderma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Troponin increased			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Failure to thrive			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			

subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Hypomagnesaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Hypoproteinaemia			
subjects affected / exposed	0 / 6 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2015	Version 2.0 • This amendment corrected that the Medical Monitor would review all available safety data bi-weekly, rather than the DMC. • This amendment corrected the dilution of MT-3724, indicating it could also be diluted in normal saline prior to infusion. • This amendment added that serum from blood samples could also be analyzed for any other anti-CD20 biologic agent which the subject may have received prior to enrolment. • A correction was made to the anticipated start of enrollment, and the addition of dose cohorts if (1) less than 2 DLTs were observed at the completion of that cohort's first cycle and (2) maximum PK/PD parameter changes had not yet been observed. • Text was added and amended to clarify the PK assessment and parameters. • Amendments were made to indicate appropriate documentation of AEs and SAEs in CRFs.
15 May 2015	Version 3.0 • This amendment changed the minimum platelet count to > 50,000/µL, because potential subjects with CTCAE v. 4.03 Grade III thrombocytopenia solely due to tumor infiltration of bone marrow and who were free of clinically significant signs/symptoms of bleeding may have experienced an increase in platelet count if the tumor cell infiltration was reduced or eliminated by MT-3724. • This amendment corrected the pre-infusion treatment for study investigators to more clearly document that they may have adjusted the recommended pre-infusion treatments (anti-pyretic, anti-histamine and glucocorticosteroids) for each subject as often as necessary based on that subject's past medical history, current medical status and/or the subject's response to one or more of the pretreatment medications.
08 July 2015	Version 4.0 • This protocol amendment enabled Investigators to enroll subjects with an expanded range of B cell hematologic malignancies (CLL/SLL) under the same investigational new drug (IND) application in one uniform clinical trial (IND#121918). • This amendment defined how further dose escalation would occur (increments of 50 µg/kg/dose), and once the maximum administered dose was identified, how dose de-escalation would occur (decrements of 25 µg/kg/dose) until the MTD was identified. The protocol retained the caveat that dose escalations was confirmed or modified by the DMC at each end-of-cohort review as the DMC reviewed the cumulative safety data across all subjects, all cohorts. • This amendment added inclusion criteria for subjects with CLL. Subjects were also required to have at least a 84 day washout (~3 half-lives for rituximab) of any prior anti-CD20 MAb therapy. • This amendment clarified the reporting requirements for SAEs. Regardless of suspected causality, SAEs were to be reported from the initiation of screening through 30 days after a subject's last dose. • This amendment updated central laboratory requirements for flow cytometry samples (a separate tube for complete blood count no longer required).

07 January 2016	Version 5.0 • This protocol amendment enabled Investigators to enroll subjects with an expanded range of B cell hematologic malignancies (CLL/SLL) under the same IND in one uniform clinical trial (IND#121918). • This amendment defined how further dose escalation would occur (increments of 50 µg/kg/dose), and once the maximum administered dose was identified, how dose de-escalation would occur (decrements of 25 µg/kg/dose) until the MTD was identified. The protocol retained the caveat that dose escalations was confirmed or modified by the DMC at each end-of-cohort review as the DMC reviewed the cumulative safety data across all subjects, all cohorts.
05 January 2017	Version 6.0 • Limited enrollment to subject with relapsed/refractory DLBCL, including those with mixed histology. • Inclusion criteria for the requirement of a rituximab sample for subjects who received rituximab within 256 days was implemented. • Added required washout for obinutuzumab, ofatumumab and ibritumomab tiuxetan • Added option for dose reduction by 25% to 33% in response to adverse event.
08 February 2018	Version 7.0 • Text was added and amended to clarify the PK assessment and parameters. • Amendments were made to indicate appropriate documentation of AEs and SAEs in CRFs.
15 April 2019	Version 7.1 • The purpose of this amendment was to add MT-3724 to be administered until disease progression, unacceptable toxicity, death, withdrawal of consent or other reason for withdrawal. The continued dosing was allowed beyond cycle 5, so subjects did not have to enroll in a separate protocol for continued dosing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 March 2021	On 19 March 2021, the US Food and Drug Administration (FDA) placed all MT-3724 IND clinical study protocols on a full hold and requested additional information. Due to the significant time needed to address the FDA requests, Molecular Templates, Inc., closed the conduct of study MT-3724_NHL_001 in all countries. Parts 1 and 2 (considered to be a Phase 1/1b of the study) were completed at the time of study closure and a full clinical study report (CSR) was prepared. Part 3 was ongoing at the time of study closure (aborted study) and only an abbreviated CSR will be prepared, and results will be added to this posting at a later date.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The phase 1 parts of this study were not designed to optimize follow-up for response, and thus there are few data points to permit definitive conclusions for efficacy.

Notes: