Clinical trial results:
Phase 1/2 Study of TAK-981 in Combination With Rituximab in Patients With Relapsed/Refractory CD20-Positive Non-Hodgkin Lymphoma

Summary

EudraCT number	2020-003946-36
Trial protocol	FR DE ES IT
Global end of trial date	26 April 2023

Results information

Result version number	v1
This version publication date	11 April 2024
First version publication date	11 April 2024

Trial information

Trial identification

Sponsor protocol code	TAK-981-1501

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04074330
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, TrialDisclosures@takeda.com
Scientific contact	Study Director, Takeda, TrialDisclosures@takeda.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	26 April 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 April 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine the safety and tolerability of TAK-981 in combination with rituximab in participants with r/r NHL.

Protection of trial subjects:

Each participant signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Japan: 4
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	38
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)	17
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 12 investigative sites in the United States, Canada, and Japan from 15 October 2019 to 26 April 2023.

Pre-assignment

Screening details:

Participants with a diagnosis of Non-Hodgkin Lymphoma were enrolled in this study consisting of Phase 1 (Dose Escalation), Phase 2 (Dose Expansion) and Japan-Specific lead-in cohort wherein participants to receive TAK-981 and rituximab.

Period 1

Period 1 title	Dose Escalation (up to 19.36 months)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: TAK-981 10mg QW

Arm description:

Participants with indolent or aggressive non-Hodgkin lymphoma (NHL) received TAK-981 10 mg, infusion, intravenously (IV), once weekly (QW) on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 milligram per square meter (mg/m^2), infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or disease progression (PD) or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Phase 1: TAK-981 40mg QW

Arm description:

Participants with indolent or aggressive NHL received TAK-981 40 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Arm type	Experimental

Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Phase 1: TAK-981 60mg QW

Arm description:

Participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Phase 1: TAK-981 90mg QW

Arm description:

Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Phase 1: TAK-981 90mg BIW

Arm description:

Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle.

Arm title	Phase 1: TAK-981 120mg QW

Arm description:

Participants with indolent or aggressive NHL received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Japan Lead-in: TAK-981 60mg QW

Arm description:

Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Japan Lead-in: TAK-981 60mg BIW

Arm description:

Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle for up to 12 months or PD or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle.

Number of subjects in period 1[1]	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW
Started	3	4	3
Completed	0	0	0
Not completed	3	4	3
Adverse event, serious fatal	-	2	-
Consent withdrawn by subject	1	1	1
Progressive Disease	2	-	-
Site Terminated by Sponsor	-	-	-
Start of New Systemic Treatment	-	-	1
Reason not Specified	-	1	1

Number of subjects in period 1[1]	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW
Started	7	8	6
Completed	0	0	0
Not completed	7	8	6
Adverse event, serious fatal	1	4	1
Consent withdrawn by subject	-	2	1
Progressive Disease	5	2	2
Site Terminated by Sponsor	-	-	1
Start of New Systemic Treatment	-	-	-
Reason not Specified	1	-	1

Number of subjects in period 1[1]	Japan Lead-in: TAK-981 60mg QW	Japan Lead-in: TAK-981 60mg BIW
Started	1	3
Completed	0	0
Not completed	1	3
Adverse event, serious fatal	-	-
Consent withdrawn by subject	-	-
Progressive Disease	1	2
Site Terminated by Sponsor	-	1
Start of New Systemic Treatment	-	-
Reason not Specified	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of participants analysed are the participants available for analyses in dose escalation period.

Period 2

Period 2 title	Dose Expansion (up to 42 months)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Phase 2 (A): TAK-981 120 mg

Arm description:

Participants with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab infusion, intravenously, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Arm title	Phase 2 (C): TAK-981 120 mg

Arm description:

Participants with follicular lymphoma (FL) received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab infusion, intravenously, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

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

Dosage and administration details:

Rituximab was administered on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Investigational medicinal product name	TAK-981
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

TAK-981 was administered on Days 1 and 8 every 21 days in each 21-day treatment cycle.

Number of subjects in period 2	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg
Started	2	1
Completed	0	0
Not completed	2	1
Adverse event, serious fatal	1	-
Study Terminated by Sponsor	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: TAK-981 10mg QW
Reporting group description:	
Participants with indolent or aggressive non-Hodgkin lymphoma (NHL) received TAK-981 10 mg, infusion, intravenously (IV), once weekly (QW) on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 milligram per square meter (mg/m^2), infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or disease progression (PD) or unacceptable toxicity.	
Reporting group title	Phase 1: TAK-981 40mg QW
Reporting group description:	
Participants with indolent or aggressive NHL received TAK-981 40 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.	
Reporting group title	Phase 1: TAK-981 60mg QW
Reporting group description:	
Participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.	
Reporting group title	Phase 1: TAK-981 90mg QW
Reporting group description:	
Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.	
Reporting group title	Phase 1: TAK-981 90mg BIW
Reporting group description:	
Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.	
Reporting group title	Phase 1: TAK-981 120mg QW
Reporting group description:	
Participants with indolent or aggressive NHL received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.	
Reporting group title	Japan Lead-in: TAK-981 60mg QW
Reporting group description:	
Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.	
Reporting group title	Japan Lead-in: TAK-981 60mg BIW
Reporting group description:	
Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle for up to 12 months or PD or unacceptable toxicity.	

Reporting group values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW
Number of subjects	3	4	3

Age Categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	64.0	69.3	73.0
full range (min-max)	56.0 to 77.0	60.0 to 80.0	67.0 to 79.0
Gender categorical Units: Subjects			
Female	1	1	1
Male	2	3	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	3	3	3
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	4	2
Unknown or Not Reported	0	0	1

Reporting group values	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW
Number of subjects	7	8	6
Age Categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	57.7	64.8	58.8
full range (min-max)	29.0 to 65.0	46.0 to 78.0	35.0 to 79.0
Gender categorical Units: Subjects			
Female	2	2	1
Male	5	6	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	7	6	6
More than one race	0	0	0
Unknown or Not Reported	0	1	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	7	7	6
Unknown or Not Reported	0	1	0

Reporting group values	Japan Lead-in: TAK-981 60mg QW	Japan Lead-in: TAK-981 60mg BIW	Total
Number of subjects	1	3	35
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	61.0	70.3	
full range (min-max)	61.0 to 61.0	68.0 to 72.0	-
Gender categorical Units: Subjects			
Female	1	3	12
Male	0	0	23
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	3	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	0	0	28
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1	3	33
Unknown or Not Reported	0	0	2

End points

End points reporting groups

Reporting group title	Phase 1: TAK-981 10mg QW

Reporting group description:

Participants with indolent or aggressive non-Hodgkin lymphoma (NHL) received TAK-981 10 mg, infusion, intravenously (IV), once weekly (QW) on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 milligram per square meter (mg/m^2), infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or disease progression (PD) or unacceptable toxicity.

Reporting group title	Phase 1: TAK-981 40mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 40 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK-981 60mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK-981 90mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK-981 90mg BIW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK-981 120mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Japan Lead-in: TAK-981 60mg QW

Reporting group description:

Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Japan Lead-in: TAK-981 60mg BIW

Reporting group description:

Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 2 (A): TAK-981 120 mg

Reporting group description:

Participants with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab infusion, intravenously, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 2 (C): TAK-981 120 mg

Reporting group description:

Participants with follicular lymphoma (FL) received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab infusion, intravenously, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Subject analysis set title	Phase 1 + Japan Lead-in: TAK-981 60mg QW
Subject analysis set type	Per protocol

Subject analysis set description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Overall number of participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

Primary: Phase 1: Number of Participants With One or More Treatment-Emergent Adverse Events (TEAEs)

End point title	Phase 1: Number of Participants With One or More Treatment-Emergent Adverse Events (TEAEs)[1][2]

End point description:

Adverse event (AE) means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. Safety Analysis Set consisted of participants who have received at least 1 dose, even if incomplete, of study drug.

End point type	Primary

End point timeframe:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

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: Descriptive data was collected and analysed only for Phase 1 arms.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	7
Units: participants	3	4	3	6

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	6		
Units: participants	8	6		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Duration of TEAEs

End point title	Phase 1: Duration of TEAEs[3][4]

End point description:

AE means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product whether or not it is related to the medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. Safety Analysis Set consisted of participants who have received at least 1 dose, even if incomplete, of study drug.

End point type	Primary

End point timeframe:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

Notes:

[3] - 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: Descriptive data was collected and analysed only for Phase 1 arms.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	8
Units: days				
median (full range (min-max))	57.0 (1 to 775)	8.0 (1 to 575)	2.0 (1 to 360)	11.0 (1 to 274)

End point values	Phase 1: TAK-981 120mg QW	Phase 1 + Japan Lead-in: TAK-981 60mg QW		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	4		
Units: days				
median (full range (min-max))	10.0 (1 to 838)	13.0 (1 to 473)		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Grade 3 or Higher TEAEs

End point title	Phase 1: Number of Participants With Grade 3 or Higher

End point description:

AE means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product whether or not it is related to the medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. A severity grade was evaluated as per the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0, except for Cytokine Release Syndrome (CRS), which was assessed by American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading criteria. Safety Analysis Set consisted of participants who have

received at least 1 dose, even if incomplete, of study drug.

End point type	Primary

End point timeframe:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

Notes:

[5] - 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: Descriptive data was collected and analysed only for Phase 1 arms.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	7
Units: participants	1	4	1	2

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	6		
Units: participants	7	3		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Overall Response Rate (ORR)

End point title	Phase 2: Overall Response Rate (ORR)[7]

End point description:

ORR was defined as the percentage of participants who achieved complete response (CR) and partial response (PR), as defined by the investigator according to Lugano classification for lymphomas during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Primary

End point timeframe:

Up to 42 months

Notes:

[7] - 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: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: percentage of participants				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs) per Dose Level

End point title	Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs) per Dose Level[8][9]

End point description:

DLTs were evaluated according to NCI CTCAE, Version 5.0. The DLT-evaluable analysis set will include participants enrolled in the Phase 1 portion of the study who experienced a DLT at any time after initiation of the first infusion of TAK-981 or who completed all planned infusions of TAK-981 as per schedule plus 3 infusions of rituximab without experiencing a DLT. Participants analyzed is the number of participants available for analysis.

End point type	Primary

End point timeframe:

Up to 42 months

Notes:

[8] - 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: Descriptive data was collected and analysed only for Phase 1 arms.

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	6
Units: participants	0	0	0	0

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax: Maximum Observed Plasma Concentration for TAK-981

End point title	Cmax: Maximum Observed Plasma Concentration for TAK-

End point description:

Pharmacokinetic (PK) analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 minutes (mins) post end of infusion (Cycle length = 21 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	7
Units: nanograms per millilitre (ng/ml)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 7, 6, 3, 4)	39.8 (± 19.1)	184 (± 139)	648 (± 214)	810 (± 305)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	51.4 (± 13.9)	200 (± 152)	600 (± 146)	967 (± 299)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: nanograms per millilitre (ng/ml)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 7, 6, 3, 4)	740 (± 491)	833 (± 73.3)	444 (± 323)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	981 (± 272)	731 (± 346)	595 (± 410)	

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax: Time of First Occurrence of the Maximum Plasma Concentration (Cmax) for TAK-981

End point title	Tmax: Time of First Occurrence of the Maximum Plasma Concentration (Cmax) for TAK-981[11]

End point description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 mins post end of infusion (Cycle length = 21 days)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	7
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n= 3, 4, 7, 7, 6, 3, 4)	1.17 (1.15 to 1.20)	1.15 (1.14 to 1.42)	1.14 (1.09 to 1.39)	1.17 (1.07 to 1.53)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	1.15 (1.07 to 1.24)	1.08 (1.04 to 1.27)	1.08 (1.02 to 1.72)	1.05 (1.00 to 1.19)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n= 3, 4, 7, 7, 6, 3, 4)	1.28 (1.10 to 1.95)	1.12 (1.12 to 1.48)	1.14 (0.97 to 1.29)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	1.11 (1.05 to 1.19)	1.12 (1.04 to 1.67)	0.95 (0.93 to 1.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-t: Area Under the Plasma Concentration-time Curve from Time 0 to Time t Over the Dosing Interval for TAK-981

End point title	AUC0-t: Area Under the Plasma Concentration-time Curve from Time 0 to Time t Over the Dosing Interval for TAK-981[12]

End point description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 mins post end of infusion (Cycle length = 21 days)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	7
Units: hours per ng/ml (h.ng/ml)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 7, 6, 3, 4)	146 (± 15.0)	477 (± 130)	1310 (± 380)	1490 (± 475)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	140 (± 25.6)	517 (± 236)	1290 (± 351)	1640 (± 483)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: hours per ng/ml (h.ng/ml)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 7, 6, 3, 4)	1640 (± 484)	1520 (± 103)	1070 (± 456)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	1780 (± 333)	1420 (± 356)	1160 (± 510)	

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-∞: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity for TAK-981

End point title	AUC0-∞: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity for TAK-981[13]

End point description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 mins post end of infusion (Cycle length = 21 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	6
Units: h.ng/ml				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	151 (± 15.1)	498 (± 128)	1360 (± 398)	1640 (± 445)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	150 (± 19.2)	538 (± 242)	1330 (± 359)	1780 (± 490)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: h.ng/ml				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	1600 (± 550)	1560 (± 114)	1110 (± 465)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	1830 (± 344)	1460 (± 382)	1210 (± 514)	

Statistical analyses

No statistical analyses for this end point

Secondary: t1/2z: Terminal Disposition Phase Half-life for TAK-981

End point title	t1/2z: Terminal Disposition Phase Half-life for TAK-981[14]

End point description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 mins post end of infusion (Cycle length = 21 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	6
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	5.06 (4.78 to 5.41)	5.88 (5.31 to 6.76)	5.75 (4.50 to 7.01)	4.88 (4.21 to 7.23)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	5.03 (3.15 to 5.92)	5.92 (5.51 to 6.15)	5.78 (4.98 to 6.29)	5.59 (3.10 to 10.93)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: hours				
median (full range (min-max))				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	5.78 (2.87 to 8.35)	5.91 (5.12 to 6.00)	6.02 (5.67 to 6.46)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	5.73 (5.23 to 6.46)	5.45 (4.16 to 6.91)	5.77 (5.12 to 7.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: CL: Total Clearance After Intravenous Administration for TAK-981

End point title	CL: Total Clearance After Intravenous Administration for TAK-981[15]

End point description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 mins post end of infusion (Cycle length = 21 days)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	6
Units: litres per hour (L/h)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	66.8 (± 6.37)	83.8 (± 17.8)	72.7 (± 27.2)	58.2 (± 15.5)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	67.4 (± 8.23)	75.2 (± 43.8)	73.3 (± 25.9)	53.9 (± 14.6)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	

Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: litres per hour (L/h)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	81.8 (± 24.7)	38.6 (± 2.78)	65.2 (± 37.0)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	68.0 (± 16.1)	43.2 (± 13.1)	57.8 (± 26.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Vss: Volume of Distribution at Steady State After Intravenous Administration for TAK-981

End point title	Vss: Volume of Distribution at Steady State After Intravenous Administration for TAK-981[16]

End point description:

PK analysis set consisted of participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Participants analyzed is the number of participants available for analysis. Number of participants analyzed is the number of participants available for analysis during the specified time-point.

End point type	Secondary

End point timeframe:

Cycle 1: Days 1 and 8, pre-infusion and at multiple timepoints (Up to 24 hours) post end of infusion; Cycle 2: Days 1 and 8, pre-infusion and at 10 mins post end of infusion (Cycle length = 21 days)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed for per dose arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 90mg QW	Phase 1: TAK-981 90mg BIW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	7	6
Units: litres (L)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	396 (± 72.8)	517 (± 202)	352 (± 136)	255 (± 75.5)
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	352 (± 79.9)	456 (± 278)	347 (± 110)	273 (± 201)

End point values	Phase 1: TAK-981 120mg QW	Japan Lead-in: TAK-981 60mg BIW	Phase 1 + Japan Lead-in: TAK-981 60mg QW	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	6	3	4	
Units: litres (L)				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n= 3, 4, 7, 6, 6, 3, 4)	410 (± 156)	154 (± 1.72)	406 (± 277)	
Cycle 1 Day 8 (n= 3, 4, 6, 5, 6, 3, 4)	307 (± 95.0)	189 (± 68.0)	332 (± 211)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Overall Response Rate (ORR)

End point title	Phase 1: Overall Response Rate (ORR)[17]

End point description:

ORR is defined as the percentage of participants who achieved CR and PR, as defined by the investigator according to Lugano classification for lymphomas during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Secondary

End point timeframe:

Up to 42 months

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	7
Units: percentage of participants				
number (not applicable)	33.3	50.0	66.7	14.3

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (not applicable)	0	33.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Duration of Response (DOR)

End point title	Phase 1: Duration of Response (DOR)[18]

End point description:

DOR is the time from the date of first documentation of a PR or better to the date of first documentation of PD for responders (PR or better). DOR was assessed by the investigator according to Lugano classification for lymphoma during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens. Participants analyzed is the number of participants with events.

End point type	Secondary

End point timeframe:

Up to 42 months

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	0[19]	0[20]	1
Units: months				
median (full range (min-max))	8.31 (8.31 to 8.31)	(to)	(to)	2.73 (2.73 to 2.73)

Notes:

[19] - Study was terminated. Please refer Global Interruption.

[20] - Study was terminated. Please refer Global Interruption.

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[21]	0[22]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[21] - Study was terminated. Please refer Global Interruption.

[22] - Study was terminated. Please refer Global Interruption.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Disease Control Rate (DCR)

End point title	Phase 1: Disease Control Rate (DCR)[23]

End point description:

DCR is defined as the percentage of participants who achieved CR, PR, and stable disease (SD) as defined by the investigator according to Lugano classification for Lymphomas during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Secondary

End point timeframe:

Up to 42 months

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	7
Units: percenage of participants				
number (not applicable)	100	50.0	100	28.6

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percenage of participants				
number (not applicable)	16.7	50.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Time to Progression (TTP)

End point title	Phase 1: Time to Progression (TTP)[24]

End point description:

TTP is defined as the time from the date of first study drug administration to the date of first documented disease progression. TTP was assessed by the investigator according to Lugano classification for lymphoma during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens. Participants analyzed is the number of participants with events. 9.9999 indicates that median was not estimable as there were censored participants with events.

End point type	Secondary

End point timeframe:

Up to 42 months

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	0[25]	0[26]	5
Units: months				
median (full range (min-max))	12.42 (2.69 to 12.42)	(to)	(to)	1.58 (0.95 to 3.98)

Notes:

[25] - Study was terminated. Please refer Global Interruption.

[26] - Study was terminated. Please refer Global Interruption.

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: months				
median (full range (min-max))	1.48 (0.00 to 3.91)	9.9999 (0.92 to 19.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Progression-Free Survival (PFS)

End point title	Phase 1: Progression-Free Survival (PFS)[27]

End point description:

PFS is defined as the time from the date of the first dose administration to the date of first documentation of PD or death due to any cause, whichever occurs first. PD was determined by Response Evaluation Criteria in Lymphoma. PFS was assessed by the investigator according to Lugano classification for lymphoma during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens. Participants analyzed are the number of participants with events. 9.9999 indicates that median was not estimable as there were censored participants with events.

End point type	Secondary

End point timeframe:

Up to 42 months

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	0[28]	0[29]	5
Units: months				
median (full range (min-max))	12.42 (2.69 to 12.42)	(to)	(to)	1.58 (1.25 to 3.98)

Notes:

[28] - Study was terminated. Please refer Global Interruption.

[29] - Study was terminated. Please refer Global Interruption.

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: months				
median (full range (min-max))	2.33 (0.43 to 3.91)	9.9999 (1.61 to 19.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Fold Change from Baseline in Levels of TAK-981-Small Ubiquitin-like Modifier (TAK-981-SUMO) Adduct Formation in Blood as Assessed by Flow Cytometry During Phase 1

End point title	Phase 1: Fold Change from Baseline in Levels of TAK-981-Small Ubiquitin-like Modifier (TAK-981-SUMO) Adduct Formation in Blood as Assessed by Flow Cytometry During Phase 1[30]

End point description:

The level of TAK-981-SUMO adduct formation was evaluated as the percentage of adduct formed in blood. Positive change denotes improvement. Pharmacodynamic analysis set consisted of participants who have provided evaluable blood samples (C1D1 predose sample and at least 1 postdose sample). Number of participants available is the number of participants with data available for analysis at the specified time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (1 hour, 4 hours, 8 hours) and Day 8 (Pre-dose, 1 hour, 4 hours and 8 hours) (Cycle length = 21 days)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	7
Units: % adduct positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /1 Hour Postdose (n=3,4,3,7,5,5)	4.1 (± 0.54)	5.7 (± 1.47)	6.3 (± 1.02)	9.5 (± 1.04)
Cycle 1 Day 1 /4 Hours Postdose (n=3,4,3,7,5,2)	3.6 (± 0.66)	4.7 (± 1.18)	4.7 (± 1.28)	6.7 (± 1.07)
Cycle 1 Day 1 /8 Hours Postdose (n=3,4,3,7,5,4)	3.7 (± 0.27)	4.5 (± 1.22)	4.1 (± 1.24)	5.6 (± 1.05)
Cycle 1 Day 8 /Predose (n=3,4,3,6,4,5)	1.8 (± 0.13)	1.9 (± 0.68)	1.9 (± 0.27)	2.5 (± 0.88)
Cycle 1 Day 8 /1 Hour Postdose (n=3,4,3,5,4,5)	4.6 (± 0.19)	6.6 (± 0.96)	8.0 (± 0.87)	9.1 (± 3.21)

Cycle 1 Day 8 /4 Hours Postdose (n=3,4,3,6,4,2)	3.9 (± 0.19)	6.2 (± 1.87)	5.1 (± 0.70)	6.1 (± 2.16)
Cycle 1 Day 8 /8 Hours Postdose (n=3,4,3,6,4,5)	3.2 (± 0.55)	4.2 (± 1.34)	4.0 (± 0.49)	5.3 (± 1.97)

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: % adduct positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /1 Hour Postdose (n=3,4,3,7,5,5)	7.6 (± 0.73)	9.9 (± 2.84)		
Cycle 1 Day 1 /4 Hours Postdose (n=3,4,3,7,5,2)	4.9 (± 1.69)	6.5 (± 0.56)		
Cycle 1 Day 1 /8 Hours Postdose (n=3,4,3,7,5,4)	4.6 (± 0.72)	5.2 (± 0.64)		
Cycle 1 Day 8 /Predose (n=3,4,3,6,4,5)	2.8 (± 0.51)	2.8 (± 1.50)		
Cycle 1 Day 8 /1 Hour Postdose (n=3,4,3,5,4,5)	7.8 (± 0.61)	11.6 (± 6.34)		
Cycle 1 Day 8 /4 Hours Postdose (n=3,4,3,6,4,2)	5.8 (± 0.65)	5.6 (± 1.73)		
Cycle 1 Day 8 /8 Hours Postdose (n=3,4,3,6,4,5)	4.0 (± 1.43)	7.1 (± 2.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Levels of TAK-981-Small Ubiquitin-like Modifier (TAK-981-SUMO) Adduct Formation in Skin as Assessed by Immunohistochemistry (IHC) During Phase 1

End point title	Phase 1: Levels of TAK-981-Small Ubiquitin-like Modifier (TAK-981-SUMO) Adduct Formation in Skin as Assessed by Immunohistochemistry (IHC) During Phase 1[31]

End point description:

The level of TAK-981-SUMO adduct formation was evaluated as the percentage of adduct formed in skin. Pharmacodynamic analysis set consisted of participants who have provided evaluable skin biopsies (screening sample and postdose sample). Participants available is the number of participants available for analysis. Number of participants available is the number of participants with data available for analysis at the specified time point. 99999 indicates that standard deviation was not estimable as there was only one participant.

End point type	Secondary

End point timeframe:

Cycle 1 Days 1 and 8 (Cycle length = 21 days)

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	6
Units: % adduct positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /Predose (n=3,4,3,6,0,4)	0.0 (± 0.03)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)
Cycle 1 Day 8 (n=3,4,3,6,1,4)	1.2 (± 1.15)	15.8 (± 12.70)	27.0 (± 12.29)	22.6 (± 9.47)

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: % adduct positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /Predose (n=3,4,3,6,0,4)	0.0 (± 0.0)	0.0 (± 0.0)		
Cycle 1 Day 8 (n=3,4,3,6,1,4)	59.7 (± 99999)	11.2 (± 11.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Fold Change from Baseline in SUMO Pathway Inhibition in Blood as Assessed by Flow Cytometry During Phase 1

End point title	Phase 1: Fold Change from Baseline in SUMO Pathway Inhibition in Blood as Assessed by Flow Cytometry During Phase 1[32]

End point description:

SUMO pathway inhibition in blood was evaluated by flow cytometry with an antibody recognizing SUMO2/3 chains. Pharmacodynamic analysis set consisted of participants who have provided evaluable blood samples (C1D1 predose sample and at least 1 postdose sample). Participants analyzed are the number of participants available for analysis. Number of participants available is the number of participants with data available for analysis at the specified time point.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (1 hour, 4 hours, 8 hours) and Day 8 (Pre-dose, 1 hour, 4 hours and 8 hours) (Cycle length = 21 days)

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	7
Units: % Sumo 2/3 positive				
arithmetic mean (standard deviation)				

Cycle 1 Day 1 /1 Hour Postdose (n=3,4,3,7,5,5)	0.9 (± 0.05)	0.8 (± 0.15)	0.5 (± 0.36)	0.6 (± 0.11)
Cycle 1 Day 1 /4 Hours Postdose (n=3,4,3,7,5,2)	0.9 (± 0.07)	0.8 (± 0.15)	0.5 (± 0.34)	0.5 (± 0.15)
Cycle 1 Day 1 /8 Hours Postdose (n=3,4,3,7,5,4)	1.0 (± 0.05)	0.8 (± 0.17)	0.5 (± 0.33)	0.5 (± 0.15)
Cycle 1 Day 8 /Predose (n=3,4,3,6,4,5)	0.9 (± 0.09)	1.1 (± 0.37)	0.8 (± 0.12)	1.1 (± 0.46)
Cycle 1 Day 8 /1 Hour Postdose (n=3,4,3,5,4,5)	0.9 (± 0.10)	0.8 (± 0.34)	0.5 (± 0.19)	0.5 (± 0.05)
Cycle 1 Day 8 /4 Hours Postdose (n=3,4,3,6,4,2)	0.9 (± 0.09)	0.7 (± 0.31)	0.5 (± 0.23)	0.6 (± 0.20)
Cycle 1 Day 8 /8 Hours Postdose (n=3,4,3,6,4,5)	0.9 (± 0.09)	0.7 (± 0.37)	0.5 (± 0.04)	0.5 (± 0.13)

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: % Sumo 2/3 positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /1 Hour Postdose (n=3,4,3,7,5,5)	0.5 (± 0.26)	0.6 (± 0.22)		
Cycle 1 Day 1 /4 Hours Postdose (n=3,4,3,7,5,2)	0.4 (± 0.30)	0.9 (± 0.14)		
Cycle 1 Day 1 /8 Hours Postdose (n=3,4,3,7,5,4)	0.5 (± 0.22)	0.7 (± 0.28)		
Cycle 1 Day 8 /Predose (n=3,4,3,6,4,5)	0.9 (± 0.07)	1.1 (± 0.25)		
Cycle 1 Day 8 /1 Hour Postdose (n=3,4,3,5,4,5)	0.5 (± 0.14)	0.6 (± 0.10)		
Cycle 1 Day 8 /4 Hours Postdose (n=3,4,3,6,4,2)	0.7 (± 0.05)	0.7 (± 0.10)		
Cycle 1 Day 8 /8 Hours Postdose (n=3,4,3,6,4,5)	0.5 (± 0.35)	0.7 (± 0.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: SUMO Pathway Inhibition in Skin as Assessed by Immunohistochemistry (IHC) During Phase 1

End point title	Phase 1: SUMO Pathway Inhibition in Skin as Assessed by Immunohistochemistry (IHC) During Phase 1[33]

End point description:

SUMO pathway inhibition in skin was evaluated with skin tissue biopsies by IHC. Pharmacodynamic analysis set consisted of participants who have provided evaluable skin biopsies (screening sample and postdose sample). Participants available is the number of participants available for analysis. Number of participants available is the number of participants with data available for analysis at the specified time point. 99999 indicates that standard deviation was not estimable as there was only one participant.

End point type	Secondary

End point timeframe:

Cycle 1 Days 1 and 8 (Cycle length = 21 days)

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive data was collected and analysed only for Phase 1 arms.

End point values	Phase 1: TAK-981 10mg QW	Phase 1: TAK-981 40mg QW	Phase 1: TAK-981 60mg QW	Phase 1: TAK-981 90mg QW
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	4	3	6
Units: % Sumo 2/3 positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /Predose (n=3,4,3,6,0,4)	83.40383 (± 2.692876)	87.7 (± 5.142812)	89.6 (± 5.528530)	89.6 (± 4.044536)
Cycle 1 Day 8 (n=3,4,3,6,1,4)	82.2 (± 2.017705)	79.3 (± 10.262143)	55.6 (± 19.325964)	52.5 (± 15.606775)

End point values	Phase 1: TAK-981 90mg BIW	Phase 1: TAK-981 120mg QW		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: % Sumo 2/3 positive				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 /Predose (n=3,4,3,6,0,4)	0.0 (± 0.0)	75.7 (± 2.586486)		
Cycle 1 Day 8 (n=3,4,3,6,1,4)	51.8 (± 99999)	63.1 (± 15.415286)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Disease Control Rate (DCR)

End point title	Phase 2: Disease Control Rate (DCR)

End point description:

CR is defined as the percentage of participants who achieved CR, PR, and SD as defined by the investigator according to Lugano classification for Lymphomas during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: percentage of participants				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants With Grade 3 or Higher TEAEs

End point title	Phase 2: Number of Participants With Grade 3 or Higher TEAEs

End point description:

AE means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product whether or not it is related to the medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. A severity grade was evaluated as per the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0, except for Cytokine Release Syndrome (CRS), which was assessed by American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading criteria. Safety Analysis Set consisted of participants who have received at least 1 dose, even if incomplete, of study drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: participants	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of TEAEs

End point title	Phase 2: Duration of TEAEs

End point description:

AE means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product whether or not it is related to the medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. Safety Analysis Set consisted of participants who have received at least 1 dose, even if incomplete, of study drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: days				
median (full range (min-max))	8.0 (1 to 483)	2.0 (1 to 349)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants With One or More Treatment-Emergent Adverse Events (TEAEs)

End point title	Phase 2: Number of Participants With One or More Treatment-Emergent Adverse Events (TEAEs)

End point description:

Adverse event (AE) means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. Safety Analysis Set consisted of participants who have received at least 1 dose, even if incomplete, of study drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: participants	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression-Free Survival (PFS)

End point title	Phase 2: Progression-Free Survival (PFS)

End point description:

PFS is defined as the time from the date of the first dose administration to the date of first documentation of PD or death due to any cause, whichever occurs first. PD was determined by Response Evaluation Criteria in Lymphoma. PFS was assessed by the investigator according to Lugano classification for lymphoma during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: months				
median (full range (min-max))	3.15 (1.0 to 5.3)	1.48 (1.48 to 1.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Progression (TTP)

End point title	Phase 2: Time to Progression (TTP)

End point description:

TTP is defined as the time from the date of first study drug administration to the date of first documented disease progression. TTP was assessed by the investigator according to Lugano classification for lymphoma during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: months				
median (full range (min-max))	5.32 (5.32 to 5.32)	1.48 (1.48 to 1.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response (DOR)

End point title	Phase 2: Duration of Response (DOR)

End point description:

DOR is the time from the date of first documentation of a PR or better to the date of first documentation of PD for responders (PR or better). DOR was assessed by the investigator according to Lugano classification for lymphoma during the study. Response-evaluable analysis set consisted of participants who have received at least 1 dose of study drug, have sites of measurable disease at Baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happens.

End point type	Secondary

End point timeframe:

Up to 42 months

End point values	Phase 2 (A): TAK-981 120 mg	Phase 2 (C): TAK-981 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: months				
median (full range (min-max))	3.32 (3.32 to 3.32)	0.03 (0.03 to 0.03)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug through 30 days after the last dose of study drug (up to 42 months)

Adverse event reporting additional description:

Safety Analysis Set consisted of participants who have received at least 1 dose, even if incomplete, of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Phase 1: TAK981 10mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 10 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK981 40mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 40 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK981 60mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK981 90mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK981 90mg BIW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 90 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Japan Lead-in: TAK981 60mg BIW

Reporting group description:

Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, BIW on Days 1, 4, 8, and 11 every 21 days in each 21-day treatment cycle for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 1: TAK981 120mg QW

Reporting group description:

Participants with indolent or aggressive NHL received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Japan Lead-in: TAK981 60mg QW

Reporting group description:

Japanese participants with indolent or aggressive NHL received TAK-981 60 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab 375 mg/m^2, infusion, IV, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 2 (A): TAK981 120mg

Reporting group description:

Participants with r/r DLBCL received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab infusion, intravenously, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Reporting group title	Phase 2 (C): TAK981 120mg

Reporting group description:

Participants with FL received TAK-981 120 mg, infusion, IV, QW on Days 1 and 8 every 21 days in each 21-day treatment cycle in combination with rituximab infusion, intravenously, once on Days 1, 8, and 15 of Cycle 1 and then on Day 1 of each 21-day treatment cycle from Cycle 2 for up to 12 months or PD or unacceptable toxicity.

Serious adverse events	Phase 1: TAK981 10mg QW	Phase 1: TAK981 40mg QW	Phase 1: TAK981 60mg QW
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Lymphoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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	1 / 3 (33.33%)	0 / 4 (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
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Large intestine perforation			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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			
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Musculoskeletal and connective tissue disorders			
Hypercreatinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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
Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (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

Serious adverse events	Phase 1: TAK981 90mg QW	Phase 1: TAK981 90mg BIW	Japan Lead-in: TAK981 60mg BIW
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	5 / 8 (62.50%)	0 / 3 (0.00%)
number of deaths (all causes)	1	4	0
number of deaths resulting from adverse events	1	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Lymphoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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 / 1	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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			
Atrial flutter			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
General physical health deterioration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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 / 7 (0.00%)	0 / 8 (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
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (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
Large intestine perforation			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Hypercreatinaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (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
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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
Musculoskeletal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (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			
Cachexia			

subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (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
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (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
Failure to thrive			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1: TAK981 120mg QW	Japan Lead-in: TAK981 60mg QW	Phase 2 (A): TAK981 120mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	1 / 2 (50.00%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Lymphoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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			
Atrial flutter			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
General physical health deterioration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (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
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Large intestine perforation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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			
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Musculoskeletal and connective tissue disorders			
Hypercreatinaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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			
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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			
Cachexia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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
Failure to thrive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (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

Serious adverse events	Phase 2 (C): TAK981 120mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphoma			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Hypercreatinaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	0 / 1 (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: 5 %

Non-serious adverse events	Phase 1: TAK981 10mg QW	Phase 1: TAK981 40mg QW	Phase 1: TAK981 60mg QW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	4 / 4 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic keratosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Superficial vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Infusion site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	2 / 3 (66.67%)
occurrences (all)	0	2	2
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Prostatomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Testicular oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal crusting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Throat irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Confusional state			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	2
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram P wave abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
QRS axis abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 3 (33.33%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin laceration			

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Thermal burn			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			

subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	2 / 3 (66.67%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Dizziness postural			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Gingival pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Oral mucosal blistering			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Toothache			

subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dermatitis bullous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lentigo			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Skin exfoliation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 4 (0.00%)	2 / 3 (66.67%)
occurrences (all)	3	0	2
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	2 / 3 (66.67%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	4	1	1
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hypercreatinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mobility decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Campylobacter colitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dehydration			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 4 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 4 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	5	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 4 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Phase 1: TAK981 90mg QW	Phase 1: TAK981 90mg BIW	Japan Lead-in: TAK981 60mg BIW
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	8 / 8 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Seborrhoeic keratosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Superficial vein thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	3 / 7 (42.86%)	3 / 8 (37.50%)	0 / 3 (0.00%)
occurrences (all)	6	3	0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Catheter site swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Infusion site reaction			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	5 / 7 (71.43%)	3 / 8 (37.50%)	2 / 3 (66.67%)
occurrences (all)	6	5	17
Peripheral swelling			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Prostatomegaly			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Testicular oedema			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 7 (14.29%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasal crusting			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pulmonary embolism			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	3 / 8 (37.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 8 (37.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Depression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood sodium decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram P wave abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	4
Platelet count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
QRS axis abnormal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	2 / 3 (66.67%)
occurrences (all)	0	1	4
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Wound haemorrhage			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Extrasystoles			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Depressed level of consciousness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dizziness postural			

subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 7 (28.57%)	4 / 8 (50.00%)	3 / 3 (100.00%)
occurrences (all)	6	4	5
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Eosinophilia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 8 (37.50%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	2 / 7 (28.57%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Abdominal distension			
subjects affected / exposed	0 / 7 (0.00%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Flatulence			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	2 / 3 (66.67%)
occurrences (all)	4	2	2
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Gingival pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 7 (28.57%)	4 / 8 (50.00%)	1 / 3 (33.33%)
occurrences (all)	2	4	1
Oral mucosal blistering			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis bullous			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	2 / 7 (28.57%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lentigo			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	1 / 3 (33.33%)
occurrences (all)	0	2	6
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercreatinaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mobility decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Bone pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteoarthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Campylobacter colitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 7 (14.29%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 8 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	2 / 7 (28.57%)	2 / 8 (25.00%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 8 (12.50%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Phase 1: TAK981 120mg QW	Japan Lead-in: TAK981 60mg QW	Phase 2 (A): TAK981 120mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	1 / 1 (100.00%)	2 / 2 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic keratosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Superficial vein thrombosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Phlebitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Chills			

subjects affected / exposed	5 / 6 (83.33%)	0 / 1 (0.00%)	2 / 2 (100.00%)
occurrences (all)	20	0	8
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Infusion site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	5 / 6 (83.33%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	10	0	0
Infusion site reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	5 / 6 (83.33%)	1 / 1 (100.00%)	2 / 2 (100.00%)
occurrences (all)	20	1	2
Peripheral swelling			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Prostatomegaly			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Testicular oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal crusting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	1
Depression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Blood sodium decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	2
CD4 lymphocytes decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	4
Ejection fraction decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram P wave abnormal			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram ST segment elevation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	2
International normalised ratio increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	1
Neutrophil count decreased			

subjects affected / exposed	1 / 6 (16.67%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
QRS axis abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	1 / 2 (50.00%)
occurrences (all)	0	2	1
Fall			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Skin laceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Thermal burn			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Wound haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Supraventricular extrasystoles			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Extrasystoles			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Depressed level of consciousness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	2
Dizziness postural			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			

subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	1
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Eosinophilia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Otorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Eye oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dysphagia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	1
Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	4	0	2
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	1
Gingival pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	1 / 2 (50.00%)
occurrences (all)	0	1	1
Oral mucosal blistering			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Dermatitis bullous			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Lentigo			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Ecchymosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Proteinuria			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	15	0	0
Back pain			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Muscle spasms			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypercreatinaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Mobility decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Bone pain			

subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Osteoarthritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 6 (0.00%)	1 / 1 (100.00%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Campylobacter colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	2	0	1
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 1 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2 (C): TAK981 120mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Seborrhoeic keratosis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Superficial vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	3		
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Phlebitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Facial pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

Chest pain				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Catheter site swelling				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Infusion site pain				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Gait disturbance				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	1 / 1 (100.00%)			
occurrences (all)	2			
Infusion site reaction				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Injection site pain				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Malaise				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Oedema peripheral				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Pyrexia				
subjects affected / exposed	1 / 1 (100.00%)			
occurrences (all)	2			
Peripheral swelling				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			

Pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Prostatomegaly			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Testicular oedema			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nasal crusting			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pleuritic pain			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Pulmonary embolism subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Throat irritation subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Confusional state subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Depression subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Blood creatinine increased			

subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Blood sodium decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
CD4 lymphocytes decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Ejection fraction decreased				
subjects affected / exposed	1 / 1 (100.00%)			
occurrences (all)	1			
Electrocardiogram P wave abnormal				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Electrocardiogram ST segment elevation				
subjects affected / exposed	1 / 1 (100.00%)			
occurrences (all)	1			
Electrocardiogram T wave abnormal				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
International normalised ratio increased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Neutrophil count decreased				
subjects affected / exposed	0 / 1 (0.00%)			
occurrences (all)	0			
Platelet count decreased				

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
QRS axis abnormal			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	2		
Fall			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin laceration			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Thermal burn			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Wound haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ventricular tachycardia			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Supraventricular extrasystoles			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Sinus bradycardia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Extrasystoles			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Atrioventricular block first degree			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Depressed level of consciousness			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dizziness postural			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

Hypoaesthesia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Lymphadenopathy			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eosinophilia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			

Otorrhoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye pruritus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Eye oedema			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dyspepsia			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Gingival pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Oral mucosal blistering			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dermatitis bullous			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

Dry skin			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Lentigo			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ecchymosis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin exfoliation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin hyperpigmentation			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Haematuria			

subjects affected / exposed occurrences (all) Pollakiuria subjects affected / exposed occurrences (all) Urinary incontinence subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Flank pain subjects affected / exposed occurrences (all) Hypercreatinaemia subjects affected / exposed occurrences (all) Mobility decreased subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Musculoskeletal chest pain	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pharyngitis streptococcal			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Campylobacter colitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypercalcaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 July 2019	The following changes were implemented as per Amendment 1: 1.Stated that a starting dose of TAK-981 that is greater than 3 mg may be considered if emerging safety data from the ongoing TAK-981-1002 single agent study supports it, and that alternative dosing schedules may be investigated. 2. Added that the approximately 34 participants in the phase 1b part of the study must be evaluable for dose-limiting toxicities, and that the approximately 56 participants in the phase 2 part of the study should be response evaluable. 3. Increased the number of sites to approximately 9 sites in phase 1b and up to approximately 20 sites total in North America and/or globally. 4. Added an appendix that defines tumor lysis syndrome (TLS). 5. Added statement that, for laboratory assessments, blood chemistries should be monitored at 6 to 8 hours and at 24 hours after the first rituximab dose, and that electrolyte abnormalities should be corrected. 6. Added statement that for participants who show evidence of prior hepatitis B infection (hepatitis B surface antigen [HBsAg] positive [regardless of antibody status] or HBsAg negative but anti-hepatitis B core antibody positive), they should consult with physicians with expertise in managing hepatitis B regarding monitoring. 7. Added that hematology/chemistry assessments should be made at end of treatment. 8. Added an appendix: Recommendations for Initial Management of Electrolyte Abnormalities and Prevention of TLS. 9. Modified inclusion criterion number 3 to require only 1 prior systemic therapy instead of 2.
26 January 2020	The following changes were implemented as per Amendment 2: 1. DLT definitions: In response to FDA's request current for clarifying the DLT criteria due to inconsistency, language was incorporated in the protocol amendment. 2. Added statement in inclusion criteria no. 11, that for fresh tumor biopsies, the lesion must be accessible for a low risk biopsy procedure. 3. Added hematology and chemistry laboratory assessments on Cycle 1 Day 1 as they are required to evaluate the suitability of TAK-981 dosing. 4. Removed window periods for tumor lysis syndrome (TLS)-related laboratory assessment. 5. Added that from Cycle 2 onwards, serum or urine pregnancy test will be performed for women of childbearing potential on Day 1 of each cycle. 6. Added statement that unless triplicate ECG are used as safety ECGs, only the general interpretation of each triplicate needs to be reported to the clinical database. 7. Stated in dose escalation (phase 1b) that the selection of the next recommended dose will be determined by the clinical study team (CST) with Bayesian Logistic Regression Modeling (BLRM) recommendations, and consideration of safety, pharmacokinetic (PK), and pharmacodynamic data, including the emerging safety, PK and pharmacodynamic data from the FIH study (TAK-981-1002). 8. Added a reference for Simon's 2-stage design for sample size determination. 9. Added window periods to biomarkers sample collection times in Schedule of Events' Table for Screening, Cycle 1 and 2 Biomarker Sample Collection. 10. Amended language for laboratory assessments under TLS management, that post dose blood chemistries will be monitored in hospitalized participants "due to high risk TLS".

18 June 2020	The following changes were implemented as per Amendment 3: 1. Updated information of the preliminary clinical experience. 2. Changed the title of the study from Phase 1b/2 to Phase 1/2. 3. Modified the Phase 2 participant population. 4. Added at least 30 additional recruiting sites and clarified that the study may be conducted outside of North America. 5. Extended the duration of the study. 6. Added an Independent Data Monitoring Committee (IDMC) to the Phase 2 study. 7. Added an Independent Review Committee (IRC) to the Phase 2 study. 8. Updated study schematic figure with the specific tumor types and indications during Phase 2. 9. Deleted measured creatinine clearance from the inclusion criterion and renal function testing. 10. Modified the inclusion criterion regarding radiologically measurable lesions. 11. Replaced Clinical Study Team (CST) with Study Monitoring Committee (SMC), and added a description of the SMC. 12. Removed LYRIC criteria for the evaluation of response. 13. Changed the window for image testing. 14. Modified the coagulation testing and urinalysis window period on Cycle 1 Day 1. 15. Changed the tumor and skin biopsy window. 16. Updated AE definition. 17. Updated serious adverse event (SAE) definition. 18. Amended the statistical description of determination of sample size for Phase 2. 19. Modified the length of infusion time. 20. Added a permitted concomitant treatment. 21. Modified the starting dose based on emerging safety data from the TAK-981-1002 single-agent study. 22. Modified the staggering period within each cohort in dose escalation. 23. Modified the grading of CRS to ASTCT Consensus Grading for CRS. 24. Updated information on Diffuse Large B-cell lymphoma. 25. Updated study objectives and endpoints. 26. Clarified exclusion criteria for participants that have undergone ASCT or cellular therapy. 27. Added text on alternative dosing schedules for TAK-981. 28. Added timepoints for serum and plasma sample collection.
19 January 2021	The following changes were implemented as per Amendment 4: 1. The creatinine clearance requirement was lowered based on recent PK analysis that showed minimal renal elimination of TAK-981. 2. In Inclusion Criterion 11, clarified that tumor biopsy collection was for participants in Phase 2, Stage 1. 3. In Exclusion Criterion 9, clarified that the washout period for prior anticancer therapy is within 2 weeks or 5 half-lives before dosing, whichever is shorter; the fragment "(up to a maximum of 4 weeks)" was deleted. 4. In Exclusion Criterion 19, added that the washout period for P-glycoprotein inhibitors is 1 week before TAK-981 dosing. 5. Updated alternative dosing schedules. 6. Clarified that body surface area used to determine rituximab dosing was to be calculated using the Du Bois formula. 7. A footnote was added to the table of chemistry and hematology tests to clarify how the units associated with collection of differential laboratory results were to be described. 8. Text defining the type of imaging assessments required at screening was added to align with the schedule of events. 9. Clarification on specimen collection during Phase 2. 10. Text was added to allow for potential remote monitoring of sites due to the COVID-19 pandemic. 11. Modifications to simplify vital signs assessment and immunesafety parameters across the TAK-981 clinical studies. 12. Alignment with recent FDA recommendations.
31 March 2021	The following changes were implemented as per Amendment 5: 1. Correction and alignment with other TAK-981 protocols. 2. Alignment of exclusion criterion in protocol summary and body. 3. Guidance on benefit/risk assessment for participant participation in the study during the COVID-19 pandemic. 4. Guidance on COVID-19 vaccination timing and procedures during the study. 5. Update to align with current Food and Drug Administration guidance.
02 September 2021	The following changes were implemented as per Amendment 6: 1. Change made to fulfill Health Authority requirement. 2. Updated pharmacology data. 3. Added nonclinical toxicology and clinical experience section with data from latest Investigator's Brochure. 4. Changes made to fulfill local requirements. 5. Update of biomarker samples collected during Phase 2. 6. Added a section defining possible reasons for study termination. 7. Updates of PK pharmacodynamic SOEs to reflect streamlined sample collection strategy in Phase 2.
04 October 2021	The following changes were implemented as per Amendment 7: 1. Correction done to align with the investigator's brochure. 2. Added additional text to include potential predictive biomarkers. 3. Modified description of countries included for conduct of study. 4. Clarification of formula-fixed, paraffin-embedded tissue block.

20 May 2022	The following changes were implemented as per Amendment 8: 1. Updated clinical experience with Phase 1 data to support the Phase 2 design. 2. Updated to provide the rationale for the 2 dose levels selected for the Phase 2 Cohorts B and C. 3. Added text noting the addition of approximately 25 participants to each of the 2 new doses within Cohorts B and C. Updated the total number of participants to 180 accordingly. 4. Updated the duration of the entire study. 5. Added information in the event of QT/corrected QT interval prolongation. 6. Added a sentence stating that pre-dose samples may be collected within up to 3 days before the visit. 7. Added wording to clarify when whole blood samples for DNA analyses are collected. 8. Bone marrow biopsy (BMB) was removed at screening; and footnote s was updated to specify BMB at investigator discretion and Lugano guidelines.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
26 April 2023	The study was terminated due to enrollment challenges.	-

Notes:

Limitations and caveats

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

The study was terminated due to enrollment challenges.

Notes: