Clinical trial results:
A Phase Ib/II Study Evaluating the Safety and Efficacy of Idasanutlin in Combination with Cytarabine and Daunorubicin in Patients Newly Diagnosed with Acute Myeloid Leukemia (AML) and the Safety and Efficacy of Idasanutlin in the Maintenance of First AML Complete Remission

Summary

EudraCT number	2018-002964-25
Trial protocol	FR ES IT
Global end of trial date	10 August 2021

Results information

Result version number	v1 (current)
This version publication date	19 September 2021
First version publication date	19 September 2021

Trial information

Trial identification

Sponsor protocol code	GO40800

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, +41
Public contact	Roche Trial Information Hotline, Roche Trial Information Hotline, +41 61 6878333,
Scientific contact	Medical Communications, Hoffmann-La Roche, CH-4070 800 8218590, genentech@druginfo.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	24 February 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 August 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

A Study Evaluating the Safety and Efficacy of Idasanutlin in Combination with Cytarabine and Daunorubicin in Patients Newly Diagnosed with Acute Myeloid Leukemia (AML) and the Safety and Efficacy of Idasanutlin in the Maintenance of First AML Complete Remission

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) guidelines according to the regulations and procedures described in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	23
EEA total number of subjects	2

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)	18
From 65 to 84 years	5

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

24 subjects were enrolled from total of 40 subjects

Pre-assignment

Screening details:

A total of 40 patients were screened; 17 patients failed the screening and 23 patients were enrolled and treated from 11 centers from the following four countries including the USA (7 Centers), Australia (2 centers), France (1 Center), and Italy (1 Center)

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose-Escalation Cohort 1

Arm description:

For maintenance, participants were treated with single agent idasanutlin of 150mg

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg idasanutlin day 1 to day 5 in combination with cytarabine 200mg day 1 to day 7 and daunorubicin 60mg day 1 to day 3 in induction

Arm title	Dose Escalation Cohort 2

Arm description:

350mg idasanutlin day 1 to day 5 in combination with cytarabine 200mg day 1 to day 7 and daunorubicin 60mg day 1 to day 3 in induction

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

350mg idasanutlin day 1 to day 5 in combination with cytarabine 200mg day 1 to day 7 and daunorubicin 60mg day 1 to day 3 in induction

Arm title	Dose Escalation Cohort 3

Arm description:

For induction, participants will be treated with 250mg idasanultin plus cytarabine. For maintenance, participants will be treated with single agent idasanutlin of 150 mg

Arm type	Experimental

Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

250mg idasanutlin day 1 to day 5 in combination with cytarabine 200mg day 1 to day 7 and daunorubicin 60mg day 1 to day 3 in induction

Arm title	Post Consolidation Cohort

Arm description:

Post consolidation cohort (experimental). 150mg idasanultin day 1 to 5 in maintenance of first remission

Arm type	Experimental
Investigational medicinal product name	Idasnutlin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150mg idasanultin day 1 to 5 in maintenance of first remission

Number of subjects in period 1	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3
Started	4	9	6
Completed	0	0	0
Not completed	4	9	6
Sponsor's decision to terminate	4	9	6

Number of subjects in period 1	Post Consolidation Cohort
Started	4
Completed	0
Not completed	4
Sponsor's decision to terminate	4

Baseline characteristics

Reporting groups	
Reporting group title	Dose-Escalation Cohort 1
Reporting group description:	
For maintenance, participants were treated with single agent idasanutlin of 150mg	
Reporting group title	Dose Escalation Cohort 2
Reporting group description:	
350mg idasanutlin day 1 to day 5 in combination with cytarabine 200mg day 1 to day 7 and daunorubicin 60mg day 1 to day 3 in induction	
Reporting group title	Dose Escalation Cohort 3
Reporting group description:	
For induction, participants will be treated with 250mg idasanultin plus cytarabine. For maintenance, participants will be treated with single agent idasanutlin of 150 mg	
Reporting group title	Post Consolidation Cohort
Reporting group description:	
Post consolidation cohort (experimental). 150mg idasanultin day 1 to 5 in maintenance of first remission	

Reporting group values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3
Number of subjects	4	9	6
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	7	6
From 65-84 years	1	2	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	49.5	45.2	49.8
standard deviation	± 17.1	± 16.9	± 14.0
Sex: Female, Male			
Units:			
Female	2	3	3
Male	2	6	3
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	3	7	4
More than one race	0	0	0

Unknown or Not Reported	1	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	5
Not Hispanic or Latino	2	9	0
Unknown or Not Reported	1	0	1

Reporting group values	Post Consolidation Cohort	Total	
Number of subjects	4	23	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	18	
From 65-84 years	2	5	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	64.8		
standard deviation	± 7.2	-	
Sex: Female, Male Units:			
Female	3	11	
Male	1	12	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	1	
White	3	17	
More than one race	0	0	
Unknown or Not Reported	1	5	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	6	
Not Hispanic or Latino	3	14	
Unknown or Not Reported	1	3	

End points

End points reporting groups

Reporting group title	Dose-Escalation Cohort 1
Reporting group description:	
For maintenance, participants were treated with single agent idasanutlin of 150mg	
Reporting group title	Dose Escalation Cohort 2
Reporting group description:	
350mg idasanutlin day 1 to day 5 in combination with cytarabine 200mg day 1 to day 7 and daunorubicin 60mg day 1 to day 3 in induction	
Reporting group title	Dose Escalation Cohort 3
Reporting group description:	
For induction, participants will be treated with 250mg idasanultin plus cytarabine. For maintenance, participants will be treated with single agent idasanutlin of 150 mg	
Reporting group title	Post Consolidation Cohort
Reporting group description:	
Post consolidation cohort (experimental). 150mg idasanultin day 1 to 5 in maintenance of first remission	

Primary: Dose Escalation Phase: Number of Participants with Dose-Limiting Toxicities (DLTs) During the First Cycle of Induction Treatment

End point title	Dose Escalation Phase: Number of Participants with Dose-Limiting Toxicities (DLTs) During the First Cycle of Induction Treatment[1]
End point description:	
Sponsor's decision to prematurely terminate the study was made at the end of Phase 1. Phase 2 was never initiated. This decision was not based on safety concerns, but rather on the overall company strategy in adult acute myeloid leukemia (AML)	
End point type	Primary
End point timeframe:	
Cycle 1 of induction treatment (1 cycle is 28 days)	

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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Participants	2	4	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with at Least One Adverse Event

End point title	Number of Participants with at Least One Adverse Event[2]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML.

End point type	Primary

End point timeframe:

From Baseline until 28 days after the final dose of study drug (up to 2 years)

Notes:

[2] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	4	9	6	4

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Grade ≥3 Adverse Events, Severity Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0)

End point title	Number of Participants with Grade ≥3 Adverse Events, Severity Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0)[3]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML.

End point type	Primary

End point timeframe:

From Baseline until 28 days after the final dose of study drug (up to 2 years)

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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Participants	4	9	5	4

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Reporting Presence or Absence of Nausea Over Time, as Assessed Through Use of the National Cancer Institute (NCI) Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE)

End point title	Number of Participants Reporting Presence or Absence of Nausea Over Time, as Assessed Through Use of the National Cancer Institute (NCI) Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE)[4]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Day 1 of each treatment cycle (1 cycle is 28 days) and at study drug discontinuation (up to 2 years)

Notes:

[4] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Reported Frequency of Nausea, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Reported Frequency of Nausea, as Assessed Through Use of the NCI PRO-CTCAE[5]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	4	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Reported Severity of Nausea, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Reported Severity of Nausea, as Assessed Through Use of the NCI PRO-CTCAE[6]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[6] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Reported Degree of Interference with Daily Function Caused by Nausea, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Reported Degree of Interference with Daily Function Caused by Nausea, as Assessed Through Use of the NCI PRO-CTCAE[7]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Overall Score for Nausea, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Overall Score for Nausea, as Assessed Through Use of the NCI PRO-CTCAE[8]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Reporting Presence or Absence of Vomiting Over Time, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Number of Participants Reporting Presence or Absence of

	Vomiting Over Time, as Assessed Through Use of the NCI PRO-CTCAE[9]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Day 1 of each treatment cycle (1 cycle is 28 days) and at study drug discontinuation (up to 2 years)

Notes:

[9] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Reported Frequency of Vomiting, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Reported Frequency of Vomiting, as Assessed Through Use of the NCI PRO-CTCAE[10]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[10] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Reported Severity of Vomiting, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Reported Severity of Vomiting, as Assessed Through Use of the NCI PRO-CTCAE[11]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[11] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Reported Degree of Interference with Daily Function Caused by Vomiting, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Reported Degree of Interference with Daily Function Caused by Vomiting, as Assessed Through Use of the NCI PRO-CTCAE[12]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[12] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline Over Time in Overall Score for Vomiting, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline Over Time in Overall Score for Vomiting, as Assessed Through Use of the NCI PRO-CTCAE[13]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[13] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Reporting Presence or Absence of Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE Over Time

End point title	Number of Participants Reporting Presence or Absence of Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE Over Time[14]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Day 1 of each treatment cycle (1 cycle is 28 days) and at study drug discontinuation (up to 2 years)

Notes:

[14] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Reported Frequency of Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline in Reported Frequency of Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE[15]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[15] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Reported Severity of Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline in Reported Severity of Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE[16]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[16] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Reported Degree of Interference with Daily Function Caused by Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline in Reported Degree of Interference with Daily Function Caused by Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE[17]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[17] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Overall Score for Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE

End point title	Change from Baseline in Overall Score for Diarrhea Over Time, as Assessed Through Use of the NCI PRO-CTCAE[18]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Primary

End point timeframe:

Baseline, Day 1 of each treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

Notes:

[18] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Complete Remission (CR) at the End of Induction Treatment, Among Those Treated at the Recommended Phase 2 Dose

End point title	Percentage of Participants with a Complete Remission (CR) at the End of Induction Treatment, Among Those Treated at the Recommended Phase 2 Dose[19]

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Partial data were available based on the evaluable data from the limited participants.

End point type	Primary

End point timeframe:

At the end of induction treatment (up to 2 cycles; 1 cycle is 28 days)

Notes:

[19] - 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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[20]	9[21]	6[22]	4[23]
Units: Percentage of Participants				
number (not applicable)				
ELN Classification: Adverse	0	25.0	100	0
ELN Classification: Favorable	0	100	66.7	0
ELN Classification: Intermediate	75.0	75.0	100	0

Notes:

[20] - ELN Adverse:0
ELN Favorable:0
ELN Intermediate:4
[21] - ELN Adverse:2
ELN Favorable:1
ELN Intermediate:4
[22] - ELN Adverse:1
ELN Favorable:3
ELN Intermediate:2
[23] - ELN Adverse:0
ELN Favorable:0
ELN Intermediate:0

Statistical analyses

No statistical analyses for this end point

Secondary: Dose Escalation and Expansion Phases: Percentage of Participants with a CR, Complete Remission with Incomplete Blood Count Recovery (CRi), or Complete Remission with Incomplete Platelet Count Recovery (CRp) at the End of Induction Treatment

End point title	Dose Escalation and Expansion Phases: Percentage of Participants with a CR, Complete Remission with Incomplete Blood Count Recovery (CRi), or Complete Remission with Incomplete Platelet Count Recovery (CRp) at the End of Induction Treatment

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

At the end of induction treatment (up to 2 cycles; 1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Dose Escalation and Expansion Phases: Percentage of Participants with a CR or Complete Remission with Partial Hematologic Recovery (CRh) at the End of Induction Treatment

End point title	Dose Escalation and Expansion Phases: Percentage of Participants with a CR or Complete Remission with Partial Hematologic Recovery (CRh) at the End of Induction Treatment

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

At the end of induction treatment (up to 2 cycles; 1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Dose-Escalation and Expansion Phases: Percentage of Participants with a Negative Minimal Residual Disease (MRD) Status at the End of Induction Treatment

End point title	Dose-Escalation and Expansion Phases: Percentage of Participants with a Negative Minimal Residual Disease (MRD) Status at the End of Induction Treatment

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

At the end of induction treatment (up to 2 cycles; 1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Post-Consolidation Phase: Percentage of Participants Converting from MRD-Positive to MRD-Negative Status at Any Time During Treatment

End point title	Post-Consolidation Phase: Percentage of Participants Converting from MRD-Positive to MRD-Negative Status at Any Time During Treatment

End point description:

Sponsor decided to not open the phase 2 portion of the study at the end of phase 1 where a RP2D was identified. This decision was not based on safety concerns, but rather on the overall company strategy in AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

At the end of maintenance treatment (12 cycles, 1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants in Event-Free Survival

End point title	Kaplan-Meier Estimate of the Percentage of Participants in Event-Free Survival

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants in Overall Survival

End point title	Kaplan-Meier Estimate of the Percentage of Participants in Overall Survival

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Percentage of Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants in Relapse-Free Survival in Those who Achieve Remission (CR, CRi, CRp, or CRh)

End point title	Kaplan-Meier Estimate of the Percentage of Participants in Relapse-Free Survival in Those who Achieve Remission (CR, CRi, CRp, or CRh)

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data

available to report.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[24]	0[25]	0[26]	0[27]
Units: Percentage of Participants				

Notes:

[24] - The study was prematurely terminated, therefore no data available

[25] - The study was prematurely terminated, therefore no data available

[26] - The study was prematurely terminated, therefore no data available

[27] - The study was prematurely terminated, therefore no data available

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in the Participant-Reported Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Questionnaire Total Score

End point title	Change from Baseline Over Time in the Participant-Reported Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Questionnaire Total Score

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle of induction and consolidation (1 cycle is 28 days), every 3 months starting at Cycle 1 of maintenance, and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[28]	0[29]	0[30]	0[31]
Units: Score				

Notes:

[28] - The study was prematurely terminated, therefore no data available

[29] - The study was prematurely terminated, therefore no data available

[30] - The study was prematurely terminated, therefore no data available

[31] - The study was prematurely terminated, therefore no data available

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in Physical Function Scale Score of the Participant-Reported European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire, Core 30 (EORTC QLQ-C30)

End point title	Change from Baseline Over Time in Physical Function Scale Score of the Participant-Reported European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire, Core 30 (EORTC QLQ-C30)

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of first induction cycle only, Day 1 of each subsequent treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[32]	0[33]	0[34]	0[35]
Units: Score				

Notes:

[32] - The study was prematurely terminated, therefore no data available

[33] - The study was prematurely terminated, therefore no data available

[34] - The study was prematurely terminated, therefore no data available

[35] - The study was prematurely terminated, therefore no data available

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in Role Function Scale Score of the Participant-Reported EORTC QLQ-C30

End point title	Change from Baseline Over Time in Role Function Scale Score of the Participant-Reported EORTC QLQ-C30

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of first induction cycle only, Day 1 of each subsequent treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[36]	0[37]	0[38]	0[39]
Units: Score				

Notes:

[36] - The study was prematurely terminated, therefore no data available

[37] - The study was prematurely terminated, therefore no data available

[38] - The study was prematurely terminated, therefore no data available

[39] - The study was prematurely terminated, therefore no data available

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in Global Health Status/Quality of Life Scale Score of the Participant-Reported EORTC QLQ-C30

End point title	Change from Baseline Over Time in Global Health Status/Quality of Life Scale Score of the Participant-Reported EORTC QLQ-C30

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of first induction cycle only, Day 1 of each subsequent treatment cycle (1 cycle is 28 days), and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in Headache Symptom Score of the Participant-Reported European Organisation for Research and Treatment of Cancer (EORTC) Item Library Questionnaire

End point title	Change from Baseline Over Time in Headache Symptom Score of the Participant-Reported European Organisation for Research and Treatment of Cancer (EORTC) Item Library Questionnaire

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall

company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle of induction and consolidation (1 cycle is 28 days), every 3 months starting at Cycle 1 of maintenance, and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in Dizziness Symptom Score of the Participant-Reported EORTC Item Library Questionnaire

End point title	Change from Baseline Over Time in Dizziness Symptom Score of the Participant-Reported EORTC Item Library Questionnaire

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle of induction and consolidation (1 cycle is 28 days), every 3 months starting at Cycle 1 of maintenance, and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in Bruising Symptom Score of the Participant-Reported EORTC Item Library Questionnaire

End point title	Change from Baseline Over Time in Bruising Symptom Score of the Participant-Reported EORTC Item Library Questionnaire

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle of induction and consolidation (1 cycle is 28 days), every 3 months starting at Cycle 1 of maintenance, and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in the European Quality of Life 5-Dimension, 5-Level Questionnaire (EQ-5D-5L) Index Utility Score

End point title	Change from Baseline Over Time in the European Quality of Life 5-Dimension, 5-Level Questionnaire (EQ-5D-5L) Index Utility Score

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of first induction cycle only, Day 1 of all cycles of consolidation (1 cycle is 28 days), every 3 months starting at Cycle 1 of maintenance, and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Over Time in the EQ-5D-5L Visual Analogue Scale (VAS) Score

End point title	Change from Baseline Over Time in the EQ-5D-5L Visual Analogue Scale (VAS) Score

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of first induction cycle only, Day 1 of all cycles of consolidation (1 cycle is 28 days), every 3 months starting at Cycle 1 of maintenance, and at study drug discontinuation (up to 2 years)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Score	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve (AUC) of Idasanutlin

End point title	Area Under the Plasma Concentration-Time Curve (AUC) of Idasanutlin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; Days 1 and 5 of consolidation Cycle 1; and Days 1 and 5 of maintenance Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: mmol/L	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Cytarabine

End point title	AUC of Cytarabine

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; and Days 1 and 5 of consolidation Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: mmol/L	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of Daunorubicin

End point title	AUC of Daunorubicin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: mmol/L	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Idasanutlin

End point title	Maximum Observed Plasma Concentration (Cmax) of Idasanutlin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; Days 1 and 5 of consolidation Cycle 1; and Days 1 and 5 of maintenance Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: ng x hr/mL	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Cytarabine

End point title	Cmax of Cytarabine

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; and Days 1 and 5 of consolidation Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: ng x hr/mL				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Daunorubicin

End point title	Cmax of Daunorubicin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: ng x hr/mL	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Total Clearance (CL) of Idasanutlin

End point title	Total Clearance (CL) of Idasanutlin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall

company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; Days 1 and 5 of consolidation Cycle 1; and Days 1 and 5 of maintenance Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Hour	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: CL of Cytarabine

End point title	CL of Cytarabine

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; and Days 1 and 5 of consolidation Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Hours	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: CL of Daunorubicin

End point title	CL of Daunorubicin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Hour	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) of Idasanutlin

End point title	Volume of Distribution at Steady State (Vss) of Idasanutlin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; Days 1 and 5 of consolidation Cycle 1; and Days 1 and 5 of maintenance Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[40]	0[41]	0[42]	0[43]
Units: Liter per Killigram				

Notes:

[40] - The study was prematurely terminated, therefore no data available

[41] - The study was prematurely terminated, therefore no data available

[42] - The study was prematurely terminated, therefore no data available

[43] - The study was prematurely terminated, therefore no data available

Statistical analyses

No statistical analyses for this end point

Secondary: Vss of Cytarabine

End point title	Vss of Cytarabine

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; and Days 1 and 5 of consolidation Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Liter per Killogram	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Vss of Daunorubicin

End point title	Vss of Daunorubicin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Liters per Kg	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-Life (t1/2) of Idasanutlin

End point title	Terminal Half-Life (t1/2) of Idasanutlin

End point description:

Sponsor decided to not open the phase 2 portion of the study at the end of phase 1 where a RP2D was identified. This decision was not based on safety concerns, but rather on the overall company strategy in AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; Days 1 and 5 of consolidation Cycle 1; and Days 1 and 5 of maintenance Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Minute	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: t1/2 of Cytarabine

End point title	t1/2 of Cytarabine

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1; and Days 1 and 5 of consolidation Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Minute	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: t1/2 of Daunorubicin

End point title	t1/2 of Daunorubicin

End point description:

Sponsor's decision to prematurely terminate the study was made at the end of the Phase 1. The planned Phase 2 was not initiated. This decision was not based on safety concerns, but rather due to the overall company strategy about the adult AML. Therefore this outcome measure was not conducted and no data available to report.

End point type	Secondary

End point timeframe:

Pre-dose and at predefined intervals post-dose on Days 1, 3, and 5 of induction Cycle 1 (1 cycle is 28 days)

End point values	Dose-Escalation Cohort 1	Dose Escalation Cohort 2	Dose Escalation Cohort 3	Post Consolidation Cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	9	6	4
Units: Minute	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to 28 days

Adverse event reporting additional description:

All AEs covered the periods of Treatment and Safety Follow-up.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	DOSE ESCALATION COHORT 1

Reporting group description:

For induction, participants will be treated with idasanutlin plus cytarabine and daunorubicin. At the investigator's discretion for consolidation, either participants will be treated with idasanutlin and cytarabine or they will undergo Allo-HSCT. For maintenance, participants will be treated with single-agent idasanutlin of 200 mg

Reporting group title	POST CONSOLIDATION PHASE COHORT

Reporting group description:

Participants who are idasanutlin treatment-naive, had received induction and chemotherapy consolidation for AML outside of the study, and were in minimal residual disease (MRD)-positive remission after induction will be enrolled in this cohort to receive maintenance treatment with single-agent idasanutlin of 150 mg

Reporting group title	DOSE ESCALATION COHORT 3

Reporting group description:

For induction, participants will be treated with idasanutlin plus cytarabine and daunorubicin. At the investigator's discretion for consolidation, either participants will be treated with idasanutlin and cytarabine or they will undergo Allo-HSCT. For maintenance, participants will be treated with single-agent idasanutlin of 250 mg

Reporting group title	DOSE ESCALATION COHORT 2

Reporting group description:

For induction, participants will be treated with idasanutlin plus cytarabine and daunorubicin. At the investigator's discretion for consolidation, either participants will be treated with idasanutlin and cytarabine or they will undergo Allo-HSCT. For maintenance, participants will be treated with single-agent idasanutlin of 350 mg

Serious adverse events	DOSE ESCALATION COHORT 1	POST CONSOLIDATION PHASE COHORT	DOSE ESCALATION COHORT 3
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Metapneumovirus infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DOSE ESCALATION COHORT 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Metapneumovirus infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	DOSE ESCALATION COHORT 1	POST CONSOLIDATION PHASE COHORT	DOSE ESCALATION COHORT 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Hypotension			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	5
Orthostatic hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	1 / 6 (16.67%)
occurrences (all)	0	5	1
Catheter site pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Catheter site erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Catheter site rash			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Chest pain			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	3 / 6 (50.00%)
occurrences (all)	2	1	4
Generalised oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Mucosal inflammation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Malaise			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	5 / 6 (83.33%)
occurrences (all)	2	0	7
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	3
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Xerosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Physical deconditioning			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Dysphonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Epistaxis			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	4
Haemoptysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pleural effusion			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pleuritic pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Sinus congestion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Upper-airway cough syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Depressed mood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	2	0	3

Suicidal ideation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	9
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	5
Bilirubin conjugated increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	4
Blood count abnormal			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood lactic acid increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood uric acid decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	5
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	8
Neutrophil count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	0	3	4
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	4
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	0	1	5
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	5
Scrotal injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			

subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Transfusion reaction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vascular access complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pericarditis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Dizziness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dizziness postural			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Headache			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Hypersomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	2 / 6 (33.33%)
occurrences (all)	5	10	4
Coagulopathy			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Febrile neutropenia			
subjects affected / exposed	3 / 4 (75.00%)	0 / 4 (0.00%)	4 / 6 (66.67%)
occurrences (all)	4	0	4
Leukopenia			
subjects affected / exposed	2 / 4 (50.00%)	3 / 4 (75.00%)	0 / 6 (0.00%)
occurrences (all)	7	14	0
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	1 / 6 (16.67%)
occurrences (all)	1	17	1
Pancytopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 4 (50.00%)	4 / 4 (100.00%)	3 / 6 (50.00%)
occurrences (all)	8	9	3

Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Ear swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Papilloedema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	4
Retinal haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	2	0	2
Abdominal pain lower			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Change of bowel habit			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	2 / 6 (33.33%)
occurrences (all)	1	2	2
Diarrhoea			
subjects affected / exposed	4 / 4 (100.00%)	3 / 4 (75.00%)	5 / 6 (83.33%)
occurrences (all)	6	5	9
Dry mouth			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	3 / 4 (75.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Gingival swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haematemesis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haematochezia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Large intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Melaena			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	4 / 4 (100.00%)	4 / 6 (66.67%)
occurrences (all)	3	6	5
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oesophageal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oesophagitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oesophagitis haemorrhagic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral disorder			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Proctalgia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	5	0	3
Tongue discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Tongue ulceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	3 / 6 (50.00%)
occurrences (all)	4	3	4
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Cholelithiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatocellular injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Angioedema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood blister			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	4
Exfoliative rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Leukoplakia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Onychalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Palmar erythema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Papule			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	5
Purpura			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	4 / 6 (66.67%)
occurrences (all)	0	2	4
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Rash morbilliform			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toxic erythema of chemotherapy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Transient acantholytic dermatosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Glycosuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Proteinuria			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gouty arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Muscle fatigue			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Neck pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Bacteroides bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Conjunctivitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Endophthalmitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Diverticulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Enterocolitis bacterial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pneumonia			

subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	1 / 6 (16.67%)
occurrences (all)	2	4	1
Fluid overload			
subjects affected / exposed	2 / 4 (50.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	15
Gout			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1

Hypoalbuminaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	7
Hypokalaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	4 / 6 (66.67%)
occurrences (all)	1	1	11
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	8
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	4 / 6 (66.67%)
occurrences (all)	0	0	6
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 6 (50.00%)
occurrences (all)	1	0	5
Metabolic acidosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	DOSE ESCALATION COHORT 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Embolism				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Flushing				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Hypertension				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Hypotension				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Orthostatic hypotension				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Catheter site pain				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Catheter site erythema				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Catheter site rash				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Chest discomfort				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Chest pain				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Chills				

subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Face oedema				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Fatigue				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
Generalised oedema				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Mucosal inflammation				
subjects affected / exposed	6 / 9 (66.67%)			
occurrences (all)	6			
Malaise				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Non-cardiac chest pain				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Oedema peripheral				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
Pain				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Peripheral swelling				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Xerosis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Physical deconditioning				

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Haemoptysis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nasal congestion			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hiccups			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pleural effusion			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Pleuritic pain			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Sneezing			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Suicidal ideation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Bilirubin conjugated increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood count abnormal			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood lactic acid increased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood uric acid decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Ejection fraction decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
International normalised ratio increased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
White blood cell count decreased			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Scrotal injury			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin abrasion			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Transfusion reaction			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Vascular access complication			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pericarditis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Sinus tachycardia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dizziness postural			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypersomnia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Restless legs syndrome			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Tremor			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Coagulopathy			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Febrile neutropenia			
subjects affected / exposed	8 / 9 (88.89%)		
occurrences (all)	11		
Leukopenia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pancytopenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Ear swelling			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Eye swelling			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Papilloedema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Periorbital oedema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Retinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	4		
Abdominal pain lower			

subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Abdominal pain upper				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Change of bowel habit				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Colitis				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
Constipation				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
Diarrhoea				
subjects affected / exposed	9 / 9 (100.00%)			
occurrences (all)	14			
Dry mouth				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Dysphagia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Gingival swelling				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Haematemesis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Haematochezia				

subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Haemorrhoids				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Hyperchlorhydria				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Ileus				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Large intestinal obstruction				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Melaena				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	8 / 9 (88.89%)			
occurrences (all)	11			
Odynophagia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Oesophageal pain				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Oesophagitis				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Oesophagitis haemorrhagic				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Oral disorder				

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Small intestinal obstruction			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Salivary hypersecretion			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Tongue discolouration			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Tongue ulceration			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	5		
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		

Cholelithiasis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hepatocellular injury			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Angioedema			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blister			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Blood blister			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Exfoliative rash			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Hyperhidrosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Leukoplakia			

subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Night sweats				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Onychalgia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Pain of skin				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Palmar erythema				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Palmar-plantar erythrodysaesthesia syndrome				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	5			
Papule				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	2			
Purpura				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	2			
Rash				
subjects affected / exposed	2 / 9 (22.22%)			
occurrences (all)	3			
Rash erythematous				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Rash macular				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			

Rash maculo-papular			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Rash morbilliform			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin fissures			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin hyperpigmentation			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Toxic erythema of chemotherapy			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Transient acantholytic dermatosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Glycosuria			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Proteinuria			

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gouty arthritis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Muscle fatigue			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Bacteraemia			

subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
COVID-19				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Bacteroides bacteraemia				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Candida infection				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Conjunctivitis				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Cystitis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Endophthalmitis				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Diverticulitis				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	1			
Enterocolitis bacterial				
subjects affected / exposed	1 / 9 (11.11%)			
occurrences (all)	2			
Influenza				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Oral candidiasis				
subjects affected / exposed	3 / 9 (33.33%)			
occurrences (all)	3			
Paronychia				
subjects affected / exposed	0 / 9 (0.00%)			
occurrences (all)	0			
Pneumonia				

subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sepsis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Fluid overload			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Gout			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypernatraemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Hypoalbuminaemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypomagnesaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	3 / 9 (33.33%)		
occurrences (all)	3		
Metabolic acidosis			
subjects affected / exposed	0 / 9 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported