Clinical trial results:
A Phase I/II, Multicenter, Open-Label, Multi-Arm Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Preliminary Activity of Idasanutlin in Combination With Either Chemotherapy or Venetoclax in the Treatment of Pediatric and Young Adult Patients With Relapsed/Refractory Acute Leukemias or Solid Tumors

Summary

EudraCT number	2018-004579-11
Trial protocol	GB FR ES NL
Global end of trial date	06 May 2024

Results information

Result version number	v2 (current)
This version publication date	09 January 2025
First version publication date	20 November 2024
Version creation reason	• Correction of full data set Updates required in one endpoint.

Trial information

Trial identification

Sponsor protocol code	GO40871

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04029688
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001489-PIP01-13
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 May 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study aims to evaluate the safety, tolerability, and pharmacokinetics (PK) of idasanutlin as a single agent and the safety, tolerability, PK, and preliminary efficacy of idasanutlin in combination with either chemotherapy or venetoclax in children and young adults with acute leukemias or solid tumors that are recurrent or refractory to standard therapy.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2020
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	United Kingdom: 13
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Canada: 1
Worldwide total number of subjects	38
EEA total number of subjects	17

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	0

months)	
Children (2-11 years)	24
Adolescents (12-17 years)	12
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with relapsed/refractory solid tumors took part in the study across 12 investigative sites in 6 countries (United States, Spain, United Kingdom, France, Canada, and Netherlands) from January 27, 2020 to May 6, 2024.

Pre-assignment

Screening details:

Study had 3 parts. Part 1a: Idasanutlin dose escalation in pediatric participants with solid tumors. Part 1b: Combination safety run-in, Part 2: Early efficacy & Part 3: Expansion in participants with neuroblastoma/acute leukemia. Leukemia cohorts in Part 1b & all cohorts in Parts 2 & 3 weren't initiated due to early study termination by sponsor.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)

Arm description:

Participants with solid tumors received idasanutlin 2 mg/kg orally once daily (QD) on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 2 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1a: Idasanutlin 3 mg/kg

Arm description:

Participants with solid tumors received idasanutlin 3 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 3 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1a: Idasanutlin 4.5 mg/kg

Arm description:

Participants with solid tumors received idasanutlin 4.5 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever

occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 4.5 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1a: Idasanutlin 6.4 mg/kg

Arm description:

Participants with solid tumors received idasanutlin 6.4 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 6.4 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1a: Idasanutlin 8 mg/kg

Arm description:

Participants with solid tumors received idasanutlin 8 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 8 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy

Arm description:

Participants with neuroblastoma received idasanutlin 2.8 mg/kg orally in combination with cyclophosphamide 200 milligrams per square meter (mg/m^2) and topotecan 0.6 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 2.8 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

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

Dosage and administration details:

Topotecan 0.6 mg/m^2 was administered as an IV infusion until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

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

Dosage and administration details:

Cyclophosphamide 200 mg/m^2 was administered as an IV infusion until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy

Arm description:

Participants with neuroblastoma received idasanutlin, 3.6 mg/kg orally, in combination with cyclophosphamide 250 mg/m^2 as and topotecan 0.75 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 3.6 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

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

Dosage and administration details:

Topotecan 0.75 mg/m^2 was administered as an IV infusion until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

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

Dosage and administration details:

Cyclophosphamide 250 mg/m^2 was administered as an IV infusion until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Arm title	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax

Arm description:

Participants with neuroblastoma (first 3) received idasanutlin, 3.6 mg/kg orally QD on Days 1-5, in combination with venetoclax 400 milligrams (mg) adult dose equivalent (adjusted by body weight) on Days 1-28 of each 28-day cycle. After the first three participants were treated, the schedule was modified as idasanutlin, 3.6 mg/kg orally QD on Days 1-5 and venetoclax 400 mg (adult dose equivalent) on Days 1-14 of a each 28-day cycle for the next 3 participants enrolled in this arm. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to

discontinue, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	
Other name	GDC-0199/ABT-0199
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Venetoclax 400 milligrams (mg) adult dose equivalent (adjusted by body weight) was administered on Days 1-28 or on Days 1-14 of each 28-day cycle.

Investigational medicinal product name	Idasanutlin
Investigational medicinal product code	RG7388; RO5503781-020
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Idasanutlin 3.6 mg/kg administered orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Number of subjects in period 1	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg
Started	8	3	6
Completed	0	0	0
Not completed	8	3	6
Consent withdrawn by subject	-	-	-
Death	8	3	6
Study Terminated by Sponsor	-	-	-

Number of subjects in period 1	Part 1a: Idasanutlin 6.4 mg/kg	Part 1a: Idasanutlin 8 mg/kg	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy
Started	3	6	3
Completed	0	0	0
Not completed	3	6	3
Consent withdrawn by subject	1	-	-
Death	2	5	-
Study Terminated by Sponsor	-	1	3

Number of subjects in period 1	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax
Started	3	6
Completed	0	0
Not completed	3	6
Consent withdrawn by subject	-	-
Death	2	3
Study Terminated by Sponsor	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)
Reporting group description:	
Participants with solid tumors received idasanutlin 2 mg/kg orally once daily (QD) on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 3 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 3 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 4.5 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 4.5 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 6.4 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 6.4 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 8 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 8 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy
Reporting group description:	
Participants with neuroblastoma received idasanutlin 2.8 mg/kg orally in combination with cyclophosphamide 200 milligrams per square meter (mg/m^2) and topotecan 0.6 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy
Reporting group description:	
Participants with neuroblastoma received idasanutlin, 3.6 mg/kg orally, in combination with cyclophosphamide 250 mg/m^2 as and topotecan 0.75 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax
Reporting group description:	
Participants with neuroblastoma (first 3) received idasanutlin, 3.6 mg/kg orally QD on Days 1-5, in combination with venetoclax 400 milligrams (mg) adult dose equivalent (adjusted by body weight) on Days 1-28 of each 28-day cycle. After the first three participants were treated, the schedule was modified as idasanutlin, 3.6 mg/kg orally QD on Days 1-5 and venetoclax 400 mg (adult dose equivalent) on Days 1-14 of a each 28-day cycle for the next 3 participants enrolled in this arm. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	

Reporting group values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg
Number of subjects	8	3	6

Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	7.6	11.3	7.3
standard deviation	± 5.0	± 3.2	± 3.9
Sex: Female, Male Units: participants			
Female	5	1	2
Male	3	2	4
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	1	0	1
White	4	2	2
More than one race	0	0	0
Unknown or Not Reported	3	1	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	1	1
Not Hispanic or Latino	3	1	2
Unknown or Not Reported	3	1	3

Reporting group values	Part 1a: Idasanutlin 6.4 mg/kg	Part 1a: Idasanutlin 8 mg/kg	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy
Number of subjects	3	6	3
Age categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	15.0	11.5	15.0
standard deviation	± 1.7	± 5.0	± 11.4
Sex: Female, Male Units: participants			
Female	1	3	1
Male	2	3	2
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	0	0
White	3	3	3
More than one race	0	0	0
Unknown or Not Reported	0	3	0

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	3	4	3
Unknown or Not Reported	0	2	0

Reporting group values	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	Total
Number of subjects	3	6	38
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	5.3	8.0	
standard deviation	± 1.2	± 3.8	-
Sex: Female, Male Units: participants			
Female	1	2	16
Male	2	4	22
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	1	0	3
White	1	3	21
More than one race	0	0	0
Unknown or Not Reported	1	3	14
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	6
Not Hispanic or Latino	2	2	20
Unknown or Not Reported	0	3	12

End points

End points reporting groups

Reporting group title	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)
Reporting group description:	
Participants with solid tumors received idasanutlin 2 mg/kg orally once daily (QD) on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 3 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 3 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 4.5 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 4.5 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 6.4 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 6.4 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1a: Idasanutlin 8 mg/kg
Reporting group description:	
Participants with solid tumors received idasanutlin 8 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy
Reporting group description:	
Participants with neuroblastoma received idasanutlin 2.8 mg/kg orally in combination with cyclophosphamide 200 milligrams per square meter (mg/m^2) and topotecan 0.6 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy
Reporting group description:	
Participants with neuroblastoma received idasanutlin, 3.6 mg/kg orally, in combination with cyclophosphamide 250 mg/m^2 as and topotecan 0.75 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Reporting group title	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax
Reporting group description:	
Participants with neuroblastoma (first 3) received idasanutlin, 3.6 mg/kg orally QD on Days 1-5, in combination with venetoclax 400 milligrams (mg) adult dose equivalent (adjusted by body weight) on Days 1-28 of each 28-day cycle. After the first three participants were treated, the schedule was modified as idasanutlin, 3.6 mg/kg orally QD on Days 1-5 and venetoclax 400 mg (adult dose equivalent) on Days 1-14 of a each 28-day cycle for the next 3 participants enrolled in this arm. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Subject analysis set title	Part 1a: Idasanutlin 3.8 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received idasanutlin 3.8 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.	
Subject analysis set title	Part 2 (Neuroblastoma)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with neuroblastoma were planned to be enrolled in various cohorts in Part 2. Participants with neuroblastoma were to receive idasanutlin in combination with cyclophosphamide 250 mg/m^2 and topotecan 0.75 mg/m^2 on Days 1-5 of each 28-day cycle or venetoclax 400 mg.

Subject analysis set title	Part 3: Expansion (Neuroblastoma)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Potential expansion of idasanutlin combination cohorts for participants with TP53 WT neuroblastoma from Parts 1b and 2, meeting the pre-defined efficacy criteria were planned to be initiated in Part 3.

Subject analysis set title	Part 1 (ALL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALL were planned to be enrolled in various cohorts in Part 1 to receive idasanutlin in combination with venetoclax 400 mg.

Subject analysis set title	Part 2 (ALL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with ALL were planned to be enrolled in Part 2 to receive idasanutlin plus venetoclax 600 mg on Days 1-5 of each 28-day cycle.

Subject analysis set title	Part 3: Expansion (ALL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Potential expansion of idasanutlin combination cohorts for participants with TP35 WT ALL from Parts 1b and 2 meeting the pre-defined efficacy criteria were planned to be initiated in Part 3.

Subject analysis set title	Part 1 (Leukemia)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) were planned to be enrolled in various cohorts in Part 1. Participants with AML and ALL were to receive idasanutlin in combination venetoclax 400 mg. Participants with AML were to receive idasanutlin plus fludarabine 30 mg/m^2 and high dose cytarabine 2000 mg/m^2 (FLA) on Days 1-5 of each 28-day cycle.

Subject analysis set title	Part 2 (Leukemia)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with AML or ALL were planned to be enrolled in various cohorts in Part 2. Participants with AML were to receive idasanutlin plus fludarabine 30 mg/m^2 and high dose cytarabine 2000 mg/m^2 (FLA) on Days 1-5 of each 28-day cycle . Participants with ALL were to receive idasanutlin plus venetoclax 600 mg on Days 1-5 of each 28-day cycle.

Subject analysis set title	Part 3: Expansion (Leukemia)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Potential expansion of idasanutlin combination cohorts for participants with TP35 WT AML or ALL from Parts 1b and 2 meeting the pre-defined efficacy criteria were planned to be initiated in Part 3.

Primary: Part 1a and 1b: Number of Participants With Adverse Events (AEs) and Severity of AEs Determined According to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5 (NCI CTCAE v5.0)

End point title	Part 1a and 1b: Number of Participants With Adverse Events (AEs) and Severity of AEs Determined According to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5 (NCI CTCAE v5.0)[1]

End point description:

AE=untoward medical occurrence in participant administered a pharmaceutical product & regardless of causal relationship with the treatment. AE=unfavorable & unintended sign, symptom/disease temporally associated with use of investigational product, whether or not considered related to it. AEs were graded per NCI CTCAE v5.0. Grade 1=Mild; asymptomatic/mild; clinical/diagnostic observations; intervention not indicated; Grade 2=Moderate; minimal, local/non-invasive intervention indicated; limiting age-appropriate instrumental activities of daily living (ADL); Grade 3=Severe/medically significant, but not

immediately life-threatening; hospitalization/prolongation of hospitalization indicated; disabling; limiting self-care ADL; Grade 4=Life-threatening consequences/urgent intervention indicated; Grade 5=Death related to AE. Safety evaluable (SE) population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Primary

End point timeframe:

From screening up to 30 days after study treatment discontinuation (approximately 7 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistics was planned for this endpoint.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	3
Units: participants				
AEs, Any Grade	8	3	6	3
AEs, Grade 1	1	0	0	0
AEs, Grade 2	0	0	0	0
AEs, Grade 3	2	1	3	2
AEs, Grade 4	5	2	3	1
AEs, Grade 5	0	0	0	0

End point values	Part 1a: Idasanutlin 8 mg/kg	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	6
Units: participants				
AEs, Any Grade	6	3	3	6
AEs, Grade 1	0	0	0	0
AEs, Grade 2	0	0	0	1
AEs, Grade 3	1	0	0	3
AEs, Grade 4	5	3	3	1
AEs, Grade 5	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Parts 1a and 1b: Number of Participants With Dose-Limiting Toxicities (DLTs)

End point title	Parts 1a and 1b: Number of Participants With Dose-Limiting Toxicities (DLTs)[2]

End point description:

DLTs were assessed for single agent idasanutlin & idasanutlin plus chemotherapy or venetoclax. DLT=AE during DLT assessment window & assessed by investigator as related/possibly related to idasanutlin. AE=untoward medical occurrence in participant administered a pharmaceutical product regardless of causal relationship with the treatment. Following events were considered DLTs: treatment-related death; elevation of serum hepatic transaminase; severe liver injury, in absence of cholestasis/other causes of hyperbilirubinemia; non-hematologic toxicity Grade ≥3; nausea, vomiting/diarrhea if Grade 3 severity lasts >than 24 hrs after initiation of supportive care measures, if Grade 4/higher; hematologic toxicity; event resulting in a dose delay beyond Day 42. DLT-evaluable population=included all participants enrolled in Part 1 who either completed at least 80% of prescribed idasanutlin dose & DLT observation window in Cycle 1 OR experienced a DLT in Cycle 1 of dose-escalation phase.

End point type	Primary

End point timeframe:

Cycle 1 (one cycle is 28 days)

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: No formal statistics was planned for this endpoint.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	3
Units: participants	0	0	1	0

End point values	Part 1a: Idasanutlin 8 mg/kg	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	6
Units: participants	4	1	2	0

Statistical analyses

No statistical analyses for this end point

Primary: Part 1b: Objective Response Rate (ORR) in Participants With TP53 Wild Type (WT) Neuroblastoma Assessed According to International Neuroblastoma Response Criteria (INRC)

End point title	Part 1b: Objective Response Rate (ORR) in Participants With TP53 Wild Type (WT) Neuroblastoma Assessed According to International Neuroblastoma Response Criteria (INRC)[3][4]

End point description:

ORR=percentage of participants with complete response (CR)/partial response (PR) at any time during study treatment, on 2 consecutive occasions ≥4 weeks apart, as determined by investigator per INRC. Primary tumor: CR= <10 millimeters(mm) residual soft tissue (ST) at primary site (PS) & complete resolution of meta-iodobenzylguanidine (MIBG)/fluorodeoxyglucose-positron emission tomography (FDG-PET) uptake at PS. PR= ≥30% decrease in longest diameter (LD) of PS & MIBG/FDG-PET uptake at PS stable, improved/resolved. ST & bone metastases: CR=resolution of all disease sites; PR=≥30% decrease in sum of non-primary target lesions, with no new lesions/≥50% reduction in MIBG score/in

number of FDG-PET–avid bone lesions; Bone marrow: CR=no tumor infiltration on reassessment. Participants in SE population with TP53 WT tumor per central testing were analyzed for this endpoint. SE population=participants who received any amount of study treatment, whether prematurely withdrawn from study/not.

End point type	Primary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

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: No formal statistics was planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	4	
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 84.19)	33.3 (0.84 to 90.37)	0 (0.0 to 60.24)	

Statistical analyses

No statistical analyses for this end point

Primary: Parts 2 and 3: ORR in Participants With TP53 WT Neuroblastoma Assessed According to INRC

End point title	Parts 2 and 3: ORR in Participants With TP53 WT Neuroblastoma Assessed According to INRC[5]

End point description:

ORR was defined as the percentage of participants with CR or PR at any time during study treatment, on 2 consecutive occasions ≥ 4 weeks apart, as determined by the investigator per INRC. Primary tumor: CR = <10 mm residual soft tissue at primary site and complete resolution of MIBG or FDG-PET uptake at primary site. PR = ≥ 30% decrease in longest diameter of primary site and MIBG or FDG-PET uptake at primary site stable, improved, or resolved. Soft tissue & bone metastases: CR = resolution of all disease sites; PR = ≥30% decrease in sum of non-primary target lesions, with no new lesions or ≥50% reduction in MIBG score or in number of FDG-PET–avid bone lesions; Bone marrow: CR = no tumor infiltration on reassessment. The study was terminated before initiation of Parts 2 and 3 as per sponsor's decision. Hence no data were collected, and this outcome measure was not assessed or analyzed.

End point type	Primary

End point timeframe:

Up to approximately 29 months

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistics was planned for this endpoint.

End point values	Part 2 (Neuroblastoma)	Part 3: Expansion (Neuroblastoma)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[6]	0[7]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[6] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

[7] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Primary: Parts 2 and 3: Minimal Residual Disease (MRD) - Negative Rate in Participants With ALL

End point title	Parts 2 and 3: Minimal Residual Disease (MRD) - Negative Rate in Participants With ALL[8]

End point description:

MRD – negative rate was defined as percentage of participants with ALL who have an MRD value < 0.01%, as measured by next-generation sequencing (NGS), within 2 cycles of study treatment. The study was terminated before initiation of Parts 2 and 3 as per sponsor's decision. Hence no data were collected, and this endpoint was not assessed or analyzed.

End point type	Primary

End point timeframe:

Up to Cycle 2 (cycle length=28 days) (approximately 8 weeks)

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: No formal statistics was planned for this endpoint.

End point values	Part 2 (ALL)	Part 3: Expansion (ALL)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[9]	0[10]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[9] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

[10] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Primary: Parts 2 and 3: Complete Remission Rate (CRR) in Participants With TP53 WT Leukemia Participants

End point title	Parts 2 and 3: Complete Remission Rate (CRR) in Participants With TP53 WT Leukemia Participants[11]

End point description:

CRR = percentage of participants with morphologic complete remission (CR), complete remission with incomplete blood count recovery (CRi), or complete remission with incomplete platelet count recovery (CRp) within 2 cycles of study treatment. CR=Bone marrow blasts <5% (AML) & no evidence of circulating blasts (ALL); absence of blasts with Auer rods (AML); absence of extramedullary disease;

absolute neutrophil count (ANC) >1.0*10^9/liter (L) [1000/microliter (µL)]; platelet count > 100*10^9/L (100,000/µL); no transfusions for a minimum of 1 week (AML and ALL). CRi= All CR criteria except for ANC <1.0*10^9/L[1000/µL] or insufficient recovery of platelet count <100* 10^9/L [100,000/µL] (AML and ALL). CRp= All CR criteria except for ANC >1.0*10^9/L[1000/µL]) or but with insufficient recovery of platelet (<100* 10^9/L [100,000/µL]) (ALL). Study was terminated before initiation of Parts 2 and 3 as per sponsor's decision. Hence no data were collected, assessed/analyzed for this endpoint.

End point type	Primary

End point timeframe:

Up to Cycle 2 (cycle length=28 days) (approximately 8 weeks)

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: No formal statistics was planned for this endpoint.

End point values	Part 2 (Leukemia)	Part 3: Expansion (Leukemia)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[12]	0[13]		
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[12] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

[13] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1a: Clinical Benefit Rate (CBR) in Participants with Solid Tumors From SE Population Assessed According to Response Evaluation Criteria Version 1.1 (RECIST v1.1) or INRC

End point title	Part 1a: Clinical Benefit Rate (CBR) in Participants with Solid Tumors From SE Population Assessed According to Response Evaluation Criteria Version 1.1 (RECIST v1.1) or INRC[14]

End point description:

CBR was defined as the percentage of participants achieving confirmed CR, PR, or stable disease (SD) on 2 consecutive occasions ≥4 weeks apart during the total study period. Per RECIST, CR was defined as the disappearance of all target lesions. PR = at least a 30% decrease in the sum of diameters (SOD) of target lesions, taking as reference the baseline SOD. SD = neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference smallest sum on study. PD = at least a 20% increase in the SOD of target lesions, taking as reference smallest sum on study (nadir), including baseline. Participants who had neuroblastoma were assessed by INRC. CR & PR per INRC were defined as outlined in the description for Part 1b: ORR endpoint. SE population = all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. Percentages have been rounded off to the nearest decimal point.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 5 (cycle length=28 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1a only.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	3
Units: percentage of participants				
number (confidence interval 95%)	12.3 (0.32 to 52.65)	33.3 (0.84 to 90.57)	0 (0.0 to 45.93)	66.7 (9.43 to 99.16)

End point values	Part 1a: Idasanutlin 8 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 45.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: CBR in Participants with Neuroblastoma From SE Population Assessed According to INRC

End point title	Part 1b: CBR in Participants with Neuroblastoma From SE Population Assessed According to INRC[15]

End point description:

CBR=percentage of participants with CR/PR/SD on 2 consecutive occasions ≥4 weeks apart per INRC. Primary tumor: CR=residual ST at PS is <10 mm, with complete resolution of MIBG/FDG-PET uptake; PR= ≥30% decrease in LD of PS, with stable/improved MIBG/FDG-PET uptake; SD=Insufficient shrinkage for PR/increase for PD. PD= >20% increase in LD from smallest sum & min. 5 mm increase in LD. ST & bone metastases: CR=resolution of all disease sites; PR=≥30% decrease in sum of non-primary target lesions with no new lesions/≥50% reduction in MIBG/number of FDG-PET–avid bone lesions; PD=new ST lesions per CT/MRI or MIBG/FDG-PET avid bone site; SD=no sufficient change in non-primary lesions. Bone marrow: CR=no tumor infiltration; PD=new tumor infiltration >5%/infiltration increased >2-fold with >20% tumor infiltration; SD=persistent infiltration at >5% w/o meeting other criteria. SE population=participants who received any amount of study treatment, whether prematurely withdrawn from study or not.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	6	
Units: percentage of participants				
number (confidence interval 95%)	33.3 (0.84 to 90.57)	33.3 (0.84 to 90.57)	0 (0.0 to 45.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: CBR in Participants With TP53 WT Neuroblastoma Assessed According to INRC

End point title	Part 1b: CBR in Participants With TP53 WT Neuroblastoma Assessed According to INRC[16]

End point description:

CBR=percentage of participants with CR/PR/SD on 2 consecutive occasions ≥4 weeks apart per INRC. Primary tumor: CR=residual ST at PS is <10 mm, with complete resolution of MIBG/FDG-PET uptake; PR= ≥30% decrease in LD of PS, with stable/improved MIBG/FDG-PET uptake; SD=Insufficient shrinkage for PR/increase for PD. PD= >20% increase in LD from smallest sum & min. 5 mm increase in LD. ST & bone metastases: CR=resolution of all disease sites; PR=≥30% decrease in sum of non-primary target lesions with no new lesions/≥50% reduction in MIBG/number of FDG-PET–avid bone lesions; PD=new ST lesions per CT/MRI or MIBG/FDG-PET avid bone site; SD=no sufficient change in non-primary lesions. Bone marrow: CR=no tumor infiltration; PD=new tumor infiltration >5%/infiltration increased >2-fold with >20% tumor infiltration; SD=persistent infiltration at >5% w/o meeting other criteria. Participants in SE population with TP53 WT tumor as assessed by central testing were analyzed for this endpoint.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	6	
Units: percentage of participants				
number (confidence interval 95%)	50.0 (1.26 to 98.74)	33.3 (0.84 to 90.57)	0 (0.0 to 60.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1a: Duration of Response (DOR) in Participants with Solid Tumors from SE Population Assessed According to RECIST v1.1 or INRC

End point title	Part 1a: Duration of Response (DOR) in Participants with Solid Tumors from SE Population Assessed According to RECIST v1.1 or INRC[17]

End point description:

DOR was defined as the time from the first tumor assessment that supports a participant's objective response (OR) (CR or PR) to the time of PD or death from any cause (whichever occurs first), as determined by the investigator using RECIST v1.1 for INRC. Per PECIST, CR was defined as disappearance of all target lesions. PR was defined as at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD. PD was defined as at least a 20% increase in the SOD of target lesions, taking as reference smallest sum on study (nadir), including baseline. Participants who had neuroblastoma were assessed by INRC. CR/PR/PD were defined per INRC as outlined in the description for the Part 1b: CBR endpoint. SE population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. DOR was only evaluated in participants who achieved an objective response (CR or PR).

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 5 (cycle length=28 days)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1a only.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	0[19]	0[20]	0[21]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[18] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.
[19] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.
[20] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.
[21] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.

End point values	Part 1a: Idasanutlin 8 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	0[22]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[22] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: DOR in Participants with Neuroblastoma From SE Population Assessed According to INRC

End point title	Part 1b: DOR in Participants with Neuroblastoma From SE Population Assessed According to INRC[23]

End point description:

DOR is the time from first tumor assessment that supports a participant's OR (CR/PR) to PD/death from any cause per INRC. Primary tumor: CR=residual ST at PS is <10 mm, with complete resolution of MIBG/FDG-PET uptake; PR= ≥30% decrease in LD of PS, with stable/improved MIBG/FDG-PET uptake; PD= >20% increase in LD from smallest sum & min. 5 mm increase in LD. ST & bone metastases: CR=resolution of all disease sites; PR=≥30% decrease in sum of non-primary target lesions with no new lesions/≥50% reduction in MIBG/number of FDG-PET–avid bone lesions; PD=new ST lesions per CT/MRI or MIBG/FDG-PET avid bone site; Bone marrow: CR=no tumor infiltration; PD=new tumor infiltration >5%/infiltration increased >2-fold with >20% tumor infiltration. SE population used. DOR was only evaluated in participants with an OR. 0.9999: Only 1 participant responded, hence the lower limit of the 95%CI is unevaluable. 9999: Only 1 participant responded, hence the upper limit of the 95%CI is unevaluable.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[24]	1	0[25]	
Units: months				
median (confidence interval 95%)	(to)	4.5 (0.99999 to 99999)	(to)	

Notes:

[24] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.
[25] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: DOR in in Participants with TP53 WT Neuroblastoma Assessed According to INRC

End point title	Part 1b: DOR in in Participants with TP53 WT Neuroblastoma Assessed According to INRC[26]

End point description:

DOR=time from initial tumor assessment of OR (CR/PR) to PD/death from any cause. Primary tumor: CR=residual ST at PS is <10 mm, with complete resolution of MIBG/FDG-PET uptake; PR= ≥30% decrease in LD of PS, with stable/improved MIBG/FDG-PET uptake; PD=>20% increase in LD from smallest sum & min. 5 mm increase in LD. ST & bone metastases: CR=resolution of all disease sites; PR=≥30% decrease in sum of non-primary target lesions with no new lesions/≥50% reduction in MIBG/number of FDG-PET–avid bone lesions; PD=new ST lesions per CT/MRI or MIBG/FDG-PET avid bone site; Bone marrow: CR=no tumor infiltration; PD=new tumor infiltration >5%/infiltration increased>2-fold with>20% tumor infiltration. Participants in the SE population with TP53 WT tumor per

central testing were analyzed. DOR was evaluated in participants with OR. 0.9999: Only 1 participant responded, so lower limit of the 95%CI is unevaluable. 9999: Only 1 participant responded, so upper limit of the 95%CI is unevaluable.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[27]	1	0[28]	
Units: months				
median (confidence interval 95%)	(to)	4.5 (0.9999 to 9999)	(to)	

Notes:

[27] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.
[28] - DOR was only evaluated in participants who achieved an OR (CR/PR). No participants achieved CR/PR.

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1a: Progression Free Survival (PFS) in Participants with Solid Tumors From SE Population Assessed According to RECIST v1.1 or INRC

End point title	Part 1a: Progression Free Survival (PFS) in Participants with Solid Tumors From SE Population Assessed According to RECIST v1.1 or INRC[29]

End point description:

PFS was defined as the time from initiation of study drug to the first documented occurrence of PD or death from any cause (whichever occurs first), as determined by the investigator using RECIST or INRC. Per RECIST, PD was defined as at least a 20% increase in the SOD of target lesions, taking as reference smallest sum on study (nadir), including baseline. Participants with neuroblastoma were assessed by INRC. PD per INRC: Primary tumor: = >20% increase in LD from smallest sum & minimum 5 mm increase in LD; Soft tissue & bone metastases =new soft tissue lesions per CT/MRI or MIBG/FDG-PET avid bone site; Bone marrow =new tumor infiltration >5% or infiltration increased >2-fold with >20% tumor infiltration. SE population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. 99999=Upper limit of the 95% CI was not estimable because there was an insufficient number of events.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 5 (cycle length=28 days)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1a only.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	3
Units: months				
median (confidence interval 95%)	0.8 (0.7 to 1.3)	0.9 (0.9 to 99999)	0.8 (0.8 to 0.9)	3.5 (2.8 to 99999)

End point values	Part 1a: Idasanutlin 8 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: months				
median (confidence interval 95%)	1.9 (0.8 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: PFS in Participants with Neuroblastoma From SE Population Assessed According to INRC

End point title	Part 1b: PFS in Participants with Neuroblastoma From SE Population Assessed According to INRC[30]

End point description:

PFS was defined as the time from initiation of study drug to the first documented occurrence of PD or death from any cause (whichever occurs first), as determined by the investigator using INRC for participants with neuroblastoma. Primary tumor: PD= >20% increase in LD from smallest sum & minimum 5 mm increase in LD. Soft tissue & bone metastases: PD=new soft tissue lesions per CT/MRI or MIBG/FDG-PET avid bone site. Bone marrow: PD=new tumor infiltration >5% or infiltration increased >2-fold with >20% tumor infiltration. Safety evaluable population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. 99999=upper limit of the 95% CI was not estimable because there was an insufficient number of events.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	6	
Units: months				
median (confidence interval 95%)	1.9 (1.8 to 99999)	1.8 (1.6 to 99999)	1.7 (1.0 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: PFS in Participants with TP53 WT Neuroblastoma Assessed According to INRC

End point title	Part 1b: PFS in Participants with TP53 WT Neuroblastoma Assessed According to INRC[31]

End point description:

PFS = the time from initiation of study drug to the first documented occurrence of PD or death from any cause (whichever occurs first), as determined by the investigator using INRC for participants with neuroblastoma. Primary tumor: PD= >20% increase in LD from smallest sum & minimum 5 mm increase in LD. Soft tissue & bone metastases: PD=new soft tissue lesions per CT/MRI or MIBG/FDG-PET avid bone site. Bone marrow: PD=new tumor infiltration >5% or infiltration increased >2-fold with >20% tumor infiltration. Participants in the SE population who had TP53 WT tumor as assessed by central testing were analyzed for this outcome measure. SE Population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. 9999=median & upper limit of the 95% CI was not estimable because there was an insufficient number of events. 99999=upper limit of the 95% CI was not estimable because there was an insufficient number of events.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	4	
Units: months				
median (confidence interval 95%)	9999 (1.8 to 9999)	1.8 (1.6 to 99999)	1.7 (1.5 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1a and 1b: Overall Survival (OS) in SE Population

End point title	Parts 1a and 1b: Overall Survival (OS) in SE Population

End point description:

OS was defined as the time from initiation of the study drug to death from any cause. SE population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. 99999=Because of the small sample size, there is not enough information to construct a reliable upper confidence limit of the 95% CI for median survival using the applied Kaplan-Meier methodology. 9999=The median, upper and lower limit of the 95% CI was not estimable because there was an insufficient number of events. 999999=The upper limit of the 95% CI was not estimable because there was an insufficient number of events.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	3
Units: months				
median (confidence interval 95%)	5.6 (2.1 to 20.8)	12.5 (1.1 to 99999)	3.6 (2.3 to 9.8)	16.4 (7.2 to 99999)

End point values	Part 1a: Idasanutlin 8 mg/kg	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	3	3	6
Units: months				
median (confidence interval 95%)	5.4 (3.4 to 999999)	9999 (9999 to 9999)	3.2 (1.6 to 99999)	99999 (2.9 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: OS in Participants With TP53 WT Neuroblastoma

End point title	Part 1b: OS in Participants With TP53 WT Neuroblastoma[32]

End point description:

OS was defined as the time from initiation of the study drug to death from any cause. Participants in the SE population who had TP53 WT tumor as assessed by central testing were analyzed for this outcome measure. SE Population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not. 9999=The median, upper and lower limit of the 95% CI was not estimable because there was an insufficient number of events. 99999=upper limit of

the 95% CI was not estimable because there was an insufficient number of events. 999=The median and upper limit of the 95% CI was not estimable because there was an insufficient number of events.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	3	4	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	3.2 (1.6 to 99999)	999 (1.5 to 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1a: ORR Irrespective of TP53 Mutation Status in Participants With Solid Tumor From SE Population According to RECIST v1.1 or INRC

End point title	Part 1a: ORR Irrespective of TP53 Mutation Status in Participants With Solid Tumor From SE Population According to RECIST v1.1 or INRC[33]

End point description:

ORR = percentage of participants with CR or PR at any time during study treatment, on two consecutive occasions ≥4 weeks apart, as determined by the investigator according to RECIST or INRC. Per RECIST, CR = disappearance of all target lesions. PR = at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD. Participants who had neuroblastoma were assessed by INRC. Per INRC, Primary tumor: CR= <10 mm residual ST at the primary site and complete resolution of MIBG/FDG-PET uptake at PS. PR= ≥30% decrease in LD of PS & MIBG/FDG-PET uptake at PS stable, improved/resolved. ST & bone metastases: CR=resolution of all disease sites; PR=≥30% decrease in sum of non-primary target lesions, with no new lesions/≥50% reduction in MIBG score/in number of FDG-PET–avid bone lesions; Bone marrow: CR=no tumor infiltration on reassessment. SE population = all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 5 (cycle length=28 days)

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1a only.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	3
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 36.94)	0 (0.0 to 70.96)	0 (0.0 to 45.93)	0 (0.0 to 70.96)

End point values	Part 1a: Idasanutlin 8 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 45.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: ORR Irrespective of TP53 Mutation Status in Participants with Neuroblastoma From SE Population according to INRC

End point title	Part 1b: ORR Irrespective of TP53 Mutation Status in Participants with Neuroblastoma From SE Population according to INRC[34]

End point description:

ORR was defined as the percentage of participants with CR or PR at any time during study treatment, on 2 consecutive occasions ≥ 4 weeks apart, as determined by the investigator per INRC. Primary tumor: CR= <10 mm residual soft tissue at primary site and complete resolution of MIBG or FDG-PET uptake at primary site. PR= ≥ 30% decrease in longest diameter of primary site and MIBG or FDG-PET uptake at primary site stable, improved, or resolved. Soft tissue & bone metastases: CR= resolution of all disease sites; PR= ≥30% decrease in sum of non-primary target lesions, with no new lesions or ≥50% reduction in MIBG score or in number of FDG-PET–avid bone lesions; Bone marrow: CR= no tumor infiltration on reassessment. SE population included all participants who received any amount of the study treatment, whether prematurely withdrawn from the study or not.

End point type	Secondary

End point timeframe:

From screening (maximum 28 days) up to Cycle 6 (cycle length=28 days)

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	6	
Units: percentage of participants				
number (confidence interval 95%)	33.3 (0.84 to 90.57)	0 (0.0 to 45.93)	0 (0.0 to 45.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1a: Maximum Plasma Concentration (Cmax) of Idasanutlin as a Monotherapy

End point title	Part 1a: Maximum Plasma Concentration (Cmax) of Idasanutlin as a Monotherapy[35]

End point description:

Pharmacokinetic (PK)-evaluable population included all participants who received at least one dose of study treatment and who have data from at least one post dose sample. One participant assigned to the 6.4 mg/kg dose level received a dose of 3.8 mg/kg due to the maximum absolute dose cap of 300 mg/day in protocol v3 and earlier. Hence this participant has been reported in a separate arm for PK analysis. 99999=Since only 1 participant was analyzed Geometric Coefficient of Variation was not estimable.

End point type	Secondary

End point timeframe:

Days 1 and 5 of Cycle 1 (cycle length = 28 days)

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1a only.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	2
Units: ng/mL(nanograms/millilitres)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	1429 (± 36)	2110 (± 27)	3174 (± 25)	4474 (± 90)
Cycle 1 Day 5	2548 (± 21)	2784 (± 27)	4892 (± 53)	7748 (± 81)

End point values	Part 1a: Idasanutlin 8 mg/kg	Part 1a: Idasanutlin 3.8 mg/kg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	1		

Units: ng/mL(nanograms/millilitres)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	5102 (± 67)	1560 (± 99999)		
Cycle 1 Day 5	6298 (± 67)	2940 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: Cmax of Idasanutlin in Combination With Chemotherapy or Venetoclax

End point title	Part 1b: Cmax of Idasanutlin in Combination With Chemotherapy or Venetoclax[36]

End point description:

PK-evaluable population included all participants who received at least one dose of study treatment and who have data from at least one post dose sample.

End point type	Secondary

End point timeframe:

Days 1 and 5 of Cycle 1 (cycle length = 28 days)

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	2834 (± 31)	1540 (± 11)	2131 (± 43)	
Cycle 1 Day 5	2393 (± 31)	2110 (± 72)	2272 (± 32)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1a: Cmax of Idasanutilin Metabolite M4 following Idasanutilin as a Monotherapy

End point title	Part 1a: Cmax of Idasanutilin Metabolite M4 following Idasanutilin as a Monotherapy[37]

End point description:

PK-evaluable population included all participants who received at least one dose of study treatment and

who have data from at least one post dose sample. One participant assigned to the 6.4 mg/kg dose level received a dose of 3.8 mg/kg due to the maximum absolute dose cap of 300 mg/day in protocol v3 and earlier. Hence this participant has been reported in a separate arm for PK analysis. 99999=Since only 1 participant was analyzed Geometric Coefficient of Variation was not estimable.

End point type	Secondary

End point timeframe:

Days 1 and 5 of Cycle 1 (cycle length = 28 days)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned for Part 1a only.

End point values	Part 1a: Idasanutlin 2 milligrams/kilograms (mg/kg)	Part 1a: Idasanutlin 3 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 6.4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	3	6	2
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	129 (± 63)	184 (± 39)	340 (± 60)	820 (± 153)
Cycle 1 Day 5	436 (± 73)	419 (± 23)	542 (± 76)	1865 (± 197)

End point values	Part 1a: Idasanutlin 8 mg/kg	Part 1a: Idasanutlin 3.8 mg/kg		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	6	1		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	575 (± 148)	72 (± 99999)		
Cycle 1 Day 5	1511 (± 201)	345 (± 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: Cmax of Idasanutlin Metabolite M4 (Idasanutilin in Combination With Chemotherapy or Venetoclax)

End point title	Part 1b: Cmax of Idasanutlin Metabolite M4 (Idasanutilin in Combination With Chemotherapy or Venetoclax)[38]

End point description:

PK-evaluable population included all participants who received at least one dose of study treatment and who have data from at least one post-dose sample.

End point type	Secondary

End point timeframe:

Days 1 and 5 of Cycle 1 (cycle length = 28 days)

Notes:

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

Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (2.8 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	6	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1	229 (± 56)	214 (± 72)	213 (± 67)	
Cycle 1 Day 5	442 (± 148)	524 (± 97)	369 (± 58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Part 1b: Plasma Concentration of Venetoclax in Combination with Idasanutlin

End point title	Part 1b: Plasma Concentration of Venetoclax in Combination with Idasanutlin[39]

End point description:

PK-evaluable population included all participants who received at least one dose of study treatment and who have data from at least one post dose sample. 'n' is the number of participants with data available for analyses at the specified timepoints.

End point type	Secondary

End point timeframe:

Cycle 1: Predose on Days 2 and 5, 4 and 6 hours post dose on Days 1 and 5 (1 cycle = 28 days)

Notes:

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

Justification: This endpoint was planned for Part 1b only.

End point values	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1, Post dose 4 Hours (n=6)	693 (± 44)			
Cycle 1 Day 1, Post dose 6 Hours (n=5)	669 (± 86)			
Cycle 1 Day 2, Predose (n=6)	202 (± 109)			
Cycle 1 Day 5, Predose (n=6)	221 (± 108)			
Cycle 1 Day 5, Post dose 4 Hours (n=6)	1145 (± 45)			

Cycle 1 Day 5, Post dose 6 Hours (n=6)	968 (± 39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1, 2 and 3: Number of Participants with Leukemia Receiving Transplant After Study Treatment

End point title	Parts 1, 2 and 3: Number of Participants with Leukemia Receiving Transplant After Study Treatment

End point description:

The study was terminated before initiation of Parts 2 and 3 as per sponsor's decision. No participants with leukemia were enrolled in Part 1. Hence no data were collected, and this outcome measure was not assessed or analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1 (Leukemia)	Part 2 (Leukemia)	Part 3: Expansion (Leukemia)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[40]	0[41]	0[42]	
Units: participants				

Notes:

[40] - No leukemia participants enrolled in Part 1.

[41] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

[42] - Study was terminated before initiation of Parts 2 & 3 per sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1, 2 and 3: Duration of Objective Response in Participants with Leukemia

End point title	Parts 1, 2 and 3: Duration of Objective Response in Participants with Leukemia

End point description:

DOR=time from 1st tumor assessment supporting OR to time of relapse/death from any cause, whichever occurs first. CR=Bone marrow blasts <5%(AML), no evidence of circulating blasts, must be <1%(ALL); absence of blasts with Auer rods(AML); absence of extramedullary disease; ANC>1.0*10^9/L [1000/µL]; platelet count>100*10^9/L (100,000/µL); independence of transfusions for a minimum of 1 week (AML &ALL). CRi=All CR criteria except for ANC <1.0*10^9/L[1000/µL] or insufficient recovery of platelet count <100*10^9/L[100,000/µL] (AML &ALL). CRp=All CR criteria except for ANC >1.0*10^9/L[1000/µL]) or but with insufficient recovery of platelet (<100*10^9/L [100,000/µL])(ALL). Relapse=participants who achieved a CR/CRp/CRi &subsequently developed: Bone marrow blasts ≥5%; reappearance of blasts in blood ≥1%; development of extra-medullary disease. No leukemia participants enrolled in Part 1. Study was terminated before Parts 2&3 initiation due to sponsors decision. Hence, no data were collected.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1 (Leukemia)	Part 2 (Leukemia)	Part 3: Expansion (Leukemia)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[43]	0[44]	0[45]	
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[43] - No leukemia participants enrolled in Part 1.

[44] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

[45] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1, 2 and 3: Event-Free Survival (EFS) in Participants with Leukemia

End point title	Parts 1, 2 and 3: Event-Free Survival (EFS) in Participants with Leukemia

End point description:

EFS=time from initiation of study drug to first documented occurrence of M3 marrow after Cycle 1, failure to achieve CR/CRp/CRi after Cycle 2, disease progression, relapse after achieving CR/CRp/CRi, or death from any cause, whichever occurs first. CR=Bone marrow blasts <5% (AML), no evidence of circulating blasts, must be <1% (ALL); absence of blasts with Auer rods (AML); absence of extramedullary disease; ANC>1.0*10^9/L [1000/µL]; platelet count>100*10^9/L (100,000/µL); independence of transfusions for a minimum of 1 week (AML & ALL). CRi=All CR criteria except for ANC <1.0*10^9/L[1000/µL] or insufficient recovery of platelet count <100*10^9/L [100,000/µL] (AML & ALL). CRp=All CR criteria except for ANC >1.0*10^9/L[1000/µL]) or but with insufficient recovery of platelet (<100*10^9/L [100,000/µL]) (ALL). Relapse=participants who achieved a CR/CRp/CRi &subsequently developed: Bone marrow blasts ≥5%; reappearance of blasts in blood ≥1%; or development of extra-medullary disease.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1 (Leukemia)	Part 2 (Leukemia)	Part 3: Expansion (Leukemia)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[46]	0[47]	0[48]	
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[46] - No leukemia participants enrolled in Part 1.

[47] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

[48] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1, 2 and 3: OS in Participants with Leukemia

End point title	Parts 1, 2 and 3: OS in Participants with Leukemia

End point description:

OS was defined as the time from initiation of study drug to death from any cause. The study was terminated before initiation of Parts 2 and 3 as per sponsor’s decision. No participants with leukemia were enrolled in Part 1. Hence no data were collected, and this outcome measure was not assessed or analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1 (Leukemia)	Part 2 (Leukemia)	Part 3: Expansion (Leukemia)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[49]	0[50]	0[51]	
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[49] - No leukemia participants enrolled in Part 1.

[50] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

[51] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1, 2 and 3: CRR of Efficacy-evaluable Population Irrespective of TP53 Mutation Status in Participants with Leukemia

End point title	Parts 1, 2 and 3: CRR of Efficacy-evaluable Population Irrespective of TP53 Mutation Status in Participants with Leukemia

End point description:

CRR was defined as the percentage of participants with CR, CRi, or CRp within 2 cycles of study treatment. CR=Bone marrow blasts <5% (AML) & no evidence of circulating blasts (ALL); absence of blasts with Auer rods (AML); absence of extramedullary disease; absolute neutrophil count (ANC) >1.0*10^9/L [1000/µL]; platelet count > 100*10^9/L (100,000/µL); no transfusions for a minimum of 1 week (AML and ALL). CRi= All CR criteria except for ANC <1.0*10^9/L[1000/µL] or insufficient recovery of platelet count <100* 10^9/L [100,000/µL] (AML and ALL). CRp=All CR criteria except for ANC >1.0*10^9/L[1000/µL]) or but with insufficient recovery of platelet (<100* 10^9/L [100,000/µL]) (ALL). The study was terminated before initiation of Parts 2 and 3 as per sponsor’s decision. No participants with leukemia were enrolled in Part 1. Hence no data were collected, and this outcome measure was not assessed or analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1 (Leukemia)	Part 2 (Leukemia)	Part 3: Expansion (Leukemia)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[52]	0[53]	0[54]	
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[52] - No leukemia participants enrolled in Part 1.

[53] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

[54] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Parts 1, 2 and 3: MRD - Negative Rate in Participants With ALL

End point title	Parts 1, 2 and 3: MRD - Negative Rate in Participants With ALL

End point description:

MRD – negative rate was defined as defined as the percentage of participants with AML who are MRD negative within 2 cycles of study treatment. The study was terminated before initiation of Parts 2 and 3 as per sponsor’s decision. No participants with leukemia were enrolled in Part 1. Hence no data were collected, and this outcome measure was not assessed or analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Part 1 (ALL)	Part 2 (ALL)	Part 3: Expansion (ALL)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[55]	0[56]	0[57]	
Units: percentage of participants				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[55] - No leukemia participants enrolled in Part 1.

[56] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

[57] - Study was terminated before initiation of Parts 2 & 3 per sponsor’s decision.

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: From screening up to 30 days after study treatment discontinuation (approximately 7 months)
All-cause mortality: From screening up to end of follow up (approximately 29 months)

Adverse event reporting additional description:

Safety population. 1 participant from idasanutlin 6.4 mg/kg arm received 3.8 mg/kg dose due to max. dose capping of 300 mg/day in protocol v3. As pre-planned, for safety evaluation & as part of modified continual reassessment method of escalation with overdose control (mCRM) review, AEs for this participant are included in the 6.4 mg/kg cohort.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Part 1a: Idasanutlin 2 mg/kg

Reporting group description:

Participants with solid tumors received idasanutlin 2 mg/kg QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1a: Idasanutlin 4.5 mg/kg

Reporting group description:

Participants with solid tumors received idasanutlin 4.5 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1a: Idasanutlin 3 mg/kg

Reporting group description:

Participants with solid tumors received idasanutlin 3 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy

Reporting group description:

Participants with neuroblastoma received idasanutlin, 3.6 mg/kg orally, in combination with cyclophosphamide 250 mg/m^2 as and topotecan 0.75 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1b: Idasanutlin (2.8mg/kg) +Chemotherapy

Reporting group description:

Participants with neuroblastoma received idasanutlin 2.8 mg/kg orally in combination with cyclophosphamide 200 mg/m^2 and topotecan 0.6 mg/m^2 as an IV infusion QD on Days 1-5 of each 28-day cycle. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1a: Idasanutlin 8 mg/kg

Reporting group description:

Participants with solid tumors received idasanutlin 8 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax

Reporting group description:

Participants with neuroblastoma (first 3) received idasanutlin, 3.6 mg/kg orally QD on Days 1-5, in combination with venetoclax 400 mg on Days 1-28 of each 28-day cycle. After the first three participants were treated, the schedule was modified as idasanutlin, 3.6 mg/kg orally QD on Days 1-5 and venetoclax 400 mg on Days 1-14 of a each 28-day cycle for the next 3 participants enrolled in this arm. Treatment was administered until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Reporting group title	Part 1a: Idasanutlin 6.4 mg/kg

Reporting group description:

Participants with solid tumors received idasanutlin 6.4 mg/kg orally QD on Days 1-5 of each 28-day cycle until disease progression, death, unacceptable toxicity, or decision to discontinue, whichever occurred first.

Serious adverse events	Part 1a: Idasanutlin 2 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 3 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	4 / 6 (66.67%)	3 / 3 (100.00%)
number of deaths (all causes)	8	6	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eschar			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 8 (37.50%)	2 / 6 (33.33%)	2 / 3 (66.67%)
occurrences causally related to treatment / all	6 / 6	3 / 3	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematotoxicity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	4 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lymphopenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	7 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	4 / 8 (50.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	7 / 7	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (2.8mg/kg) +Chemotherapy	Part 1a: Idasanutlin 8 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	6 / 6 (100.00%)
number of deaths (all causes)	2	0	5
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Eschar			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Cardiac disorders			
Sinus tachycardia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Partial seizures			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	3 / 6 (50.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Haematotoxicity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Stomatitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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			
Bacteraemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (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
Appendicitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Central nervous system infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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	0 / 3 (0.00%)	0 / 3 (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
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (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

Serious adverse events	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	Part 1a: Idasanutlin 6.4 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	2 / 3 (66.67%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Asthma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eschar			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Headache			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematotoxicity			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1a: Idasanutlin 2 mg/kg	Part 1a: Idasanutlin 4.5 mg/kg	Part 1a: Idasanutlin 3 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	6 / 6 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 8 (37.50%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	5	3	1
Asthenia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Mucosal inflammation			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Non-cardiac chest pain			

subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	5
Pain			
subjects affected / exposed	1 / 8 (12.50%)	3 / 6 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	4	1
Pyrexia			
subjects affected / exposed	3 / 8 (37.50%)	2 / 6 (33.33%)	3 / 3 (100.00%)
occurrences (all)	3	3	3
Vascular device occlusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Wheezing			

subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Confusional state			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 8 (50.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood chloride decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Weight decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

SARS-CoV-2 test positive			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Pelvic fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Accidental overdose			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Seizure			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	5	2	0
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 8 (50.00%)	3 / 6 (50.00%)	2 / 3 (66.67%)
occurrences (all)	5	4	2
Febrile neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	2	1
Lymphopenia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Leukopenia			
subjects affected / exposed	3 / 8 (37.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 8 (37.50%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	2
Constipation			

subjects affected / exposed	1 / 8 (12.50%)	2 / 6 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	2	4
Diarrhoea			
subjects affected / exposed	3 / 8 (37.50%)	5 / 6 (83.33%)	1 / 3 (33.33%)
occurrences (all)	4	7	3
Gastritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lip swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	3
Stomatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	4 / 8 (50.00%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	7	9	8
Nausea			
subjects affected / exposed	3 / 8 (37.50%)	4 / 6 (66.67%)	2 / 3 (66.67%)
occurrences (all)	4	6	6
Anal fissure			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Haematochezia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Mouth swelling			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Erythema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Livedo reticularis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Purpura			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
COVID-19			

subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Device related infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Lymphangitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	2 / 6 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	3	2
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hypocalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1b: Idasanutlin (3.6 mg/kg) +Chemotherapy	Part 1b: Idasanutlin (2.8mg/kg) +Chemotherapy	Part 1a: Idasanutlin 8 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vascular device occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Rhinorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypoxia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	1 / 6 (16.67%)
occurrences (all)	6	2	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	1 / 6 (16.67%)
occurrences (all)	6	2	1
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	3 / 3 (100.00%)	2 / 3 (66.67%)	0 / 6 (0.00%)
occurrences (all)	5	2	0
Blood chloride decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	0 / 6 (0.00%)
occurrences (all)	1	4	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Neutrophil count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
White blood cell count decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	3	0	2

Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pelvic fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Seizure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	6 / 6 (100.00%)
occurrences (all)	9	4	6
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	3 / 6 (50.00%)
occurrences (all)	2	7	3
Lymphopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	2
Neutropenia			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	1 / 6 (16.67%)
occurrences (all)	3	10	1
Leukopenia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 3 (100.00%)	0 / 6 (0.00%)
occurrences (all)	3	8	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 6 (16.67%)
occurrences (all)	4	1	1
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	7	1	2
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	3 / 6 (50.00%)
occurrences (all)	5	0	3
Anal fissure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Mouth swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Skin hyperpigmentation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pain of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Livedo reticularis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphangitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Hypokalaemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Hyponatraemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	9	0	1
Hypoalbuminaemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 1b: Idasanutlin (3.6mg/kg) + Venetoclax	Part 1a: Idasanutlin 6.4 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	3 / 3 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Asthenia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Vascular device occlusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Swelling			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	2	
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Asthma			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tachypnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)		
occurrences (all)	2	0		
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Blood bicarbonate increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Blood bilirubin increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Blood chloride decreased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Platelet count decreased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Blood uric acid increased				
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)		
occurrences (all)	1	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Lymphocyte count decreased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Neutrophil count decreased				
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)		
occurrences (all)	1	0		
Blood creatinine increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)		
occurrences (all)	0	0		
Weight decreased				
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)		
occurrences (all)	1	0		

White blood cell count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood phosphorus decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pelvic fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Accidental overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Seizure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Paraesthesia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Febrile neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	2	1	
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Leukopenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Periorbital oedema			

subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	3 / 3 (100.00%)	
occurrences (all)	1	4	
Gastritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Lip swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oral pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	4 / 6 (66.67%)	1 / 3 (33.33%)	
occurrences (all)	7	3	
Nausea			
subjects affected / exposed	5 / 6 (83.33%)	2 / 3 (66.67%)	
occurrences (all)	6	2	
Anal fissure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	

Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Mouth swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin hyperpigmentation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pain of skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Livedo reticularis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Purpura			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			

Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Skin infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Upper respiratory tract infection			

subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Mucosal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Device related infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Fungal skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Lymphangitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Parainfluenzae virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 6 (33.33%)	0 / 3 (0.00%)	
occurrences (all)	2	0	

Hyperglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2020	1. The primary efficacy objective endpoint for leukemia for participants with ALL was clarified. 2. The DLTs definitions were revised. 3. Because no assessments of peripheral blood mononuclear cells were planned, sampling of these for biomarkers assessment was removed. 4. Administration of idasanutlin via nasogastric tube was added for participants receiving idasanutlin tablets dissolved in water. 5. Risks associated with venetoclax were updated.
19 March 2021	1. Initiation of the safety run-in cohorts for the planned combinations in neuroblastoma may occur asynchronously. Thus, the randomization of participants with neuroblastoma in study Part 2 to either chemotherapy or venetoclax was removed. 2. An early efficacy gate was added at the end of the safety run-in (Gate 1b) for the neuroblastoma cohorts, which included participants treated at the recommended Phase II dose (RP2D). 4. A requirement for a minimum of 6 participants treated at the RP2D in neuroblastoma safety run-in was added. 5. The pre-defined maximum dose of idasanutlin was eliminated. 6. The definition of dose-limiting toxicities was revised to accommodate the known and manageable toxicities of the chemotherapy combination agents, as well as to be more consistent with the standards used in other pediatric clinical trials. 7. The inclusion criterion on the ability to swallow tablets or liquid was removed since the administration of idasanutlin via nasogastric tube is possible. 8. Dosing of topotecan and cyclophosphamide based on body weight rather than body surface area for patients weighing less than 12 kg. This is more consistent with standard dosing for this regimen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported