Clinical trial results:
A Phase 1/2 Study of ARQ 092 (Miransertib) in Subjects with PIK3CA-related Overgrowth Spectrum and Proteus Syndrome

Summary

EudraCT number	2016-000558-37
Trial protocol	IT FR ES GB DE
Global end of trial date	11 April 2022

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	7075-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03094832
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Protocol Number: MK-7075-002

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 April 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 April 2022
Global end of trial reached?	Yes
Global end of trial date	11 April 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

In this study, oral miransertib (MK-7075, formerly called ARQ 092) was administered to participants at least 2 years of age with phosphatidylinositol-4,5-bisphosphate 3 kinase, catalytic subunit alpha (PIK3CA)-related Overgrowth Spectrum (PROS) and Proteus Syndrome (PS) (MOSAIC). The study consists of two parts: Part A and Part B. In Part A, participants with either PROS or PS received miransertib orally once daily (QD) for first 3 cycles (each cycle length=28 days) with an option to increase the dose at the investigator's discretion. Part A was closed to enrollment under Amendment 6. In Part B Cohorts 1, 2, and 3 participants received a starting dose of miransertib QD for the first 3 cycles and then the dose was increased at the investigator's discretion, provided no clinically significant drug related toxicity was observed. In Part B Cohort 4 participants previously treated with miransertib or currently receiving miransertib were enrolled under Compassionate Use/Expanded Access.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	50
EEA total number of subjects	13

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)	29
Adolescents (12-17 years)	13
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

50 participants were enrolled in the study of which 49 participants received at least one dose of treatment and was used for safety analysis.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Miransertib PROS/PS

Arm description:

During Cycles 1-3, participants with either PROS (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha [PIK3CA]-related Overgrowth Spectrum) or PS (Proteus syndrome) received miransertib 15 mg/m^2 once daily (QD) (each cycle length = 28 days). From Cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 and then titrated to 35 mg/m^2 orally QD at the investigator’s discretion.

Arm type	Experimental
Investigational medicinal product name	Miransertib
Investigational medicinal product code	
Other name	MK-7075, ARQ 092
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Initial dose of 15 mg/m^2 or 25 mg/m^2 orally QD and then titrated up to 25 mg/m^2 or 35 mg/m^2 orally QD at the investigator's discretion.

Arm title	Part B: Miransertib PROS (Cohort 1)

Arm description:

During Cycles 1-3, participants with PROS who have a measurable lesion by volumetric magnetic resonance imaging (MRI) received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Miransertib
Investigational medicinal product code	
Other name	MK-7075, ARQ 092
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Initial dose of 15 mg/m^2 or 25 mg/m^2 orally QD and then titrated up to 25 mg/m^2 or 35 mg/m^2 orally QD at the investigator's discretion.

Arm title	Part B: Miransertib PS (Cohort 2)

Arm description:

During Cycles 1-3, participants with PS who have a measurable lesion by standardized digital photography received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Miransertib
Investigational medicinal product code	
Other name	MK-7075, ARQ 092
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Initial dose of 15 mg/m^2 or 25 mg/m^2 orally QD and then titrated up to 25 mg/m^2 or 35 mg/m^2 orally QD at the investigator's discretion.

Arm title	Part B: Miransertib PROS/PS (Cohort 3)

Arm description:

During Cycles 1-3, participants with PROS or PS who do not meet all the eligibility criteria for Cohorts 1 or 2 received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Arm type	Experimental
Investigational medicinal product name	Miransertib
Investigational medicinal product code	
Other name	MK-7075, ARQ 092
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Initial dose of 15 mg/m^2 or 25 mg/m^2 orally QD and then titrated up to 25 mg/m^2 or 35 mg/m^2 orally QD at the investigator's discretion.

Arm title	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)

Arm description:

During cycles 1-48 (each cycle length = 28 days) or until disease progression, unacceptable toxicity, or discontinuation, participants previously treated with miransertib or currently receiving miransertib under Compassionate Use/Expanded Access continued to receive the current dose of miransertib (did not exceed 25 mg/m^2).

Arm type	Experimental
Investigational medicinal product name	Miransertib
Investigational medicinal product code	
Other name	MK-7075, ARQ 092
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Initial dose of 15 mg/m^2 or 25 mg/m^2 orally QD and then titrated up to 25 mg/m^2 or 35 mg/m^2 orally QD at the investigator's discretion.

Number of subjects in period 1	Part A: Miransertib PROS/PS	Part B: Miransertib PROS (Cohort 1)	Part B: Miransertib PS (Cohort 2)
Started	17	22	1
Treated	17	22	1
Completed	2	2	0
Not completed	15	20	1
Other	13	20	1
Death	1	-	-
Withdrawal by Parent/Guardian	1	-	-

Lost to follow-up	-	-	-

Number of subjects in period 1	Part B: Miransertib PROS/PS (Cohort 3)	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)
Started	8	2
Treated	8	1
Completed	0	0
Not completed	8	2
Other	7	1
Death	-	-
Withdrawal by Parent/Guardian	-	-
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Part A: Miransertib PROS/PS
Reporting group description:	
During Cycles 1-3, participants with either PROS (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha [PIK3CA]-related Overgrowth Spectrum) or PS (Proteus syndrome) received miransertib 15 mg/m^2 once daily (QD) (each cycle length = 28 days). From Cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 and then titrated to 35 mg/m^2 orally QD at the investigator's discretion.	
Reporting group title	Part B: Miransertib PROS (Cohort 1)
Reporting group description:	
During Cycles 1-3, participants with PROS who have a measurable lesion by volumetric magnetic resonance imaging (MRI) received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.	
Reporting group title	Part B: Miransertib PS (Cohort 2)
Reporting group description:	
During Cycles 1-3, participants with PS who have a measurable lesion by standardized digital photography received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.	
Reporting group title	Part B: Miransertib PROS/PS (Cohort 3)
Reporting group description:	
During Cycles 1-3, participants with PROS or PS who do not meet all the eligibility criteria for Cohorts 1 or 2 received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.	
Reporting group title	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)
Reporting group description:	
During cycles 1-48 (each cycle length = 28 days) or until disease progression, unacceptable toxicity, or discontinuation, participants previously treated with miransertib or currently receiving miransertib under Compassionate Use/Expanded Access continued to receive the current dose of miransertib (did not exceed 25 mg/m^2).	

Reporting group values	Part A: Miransertib PROS/PS	Part B: Miransertib PROS (Cohort 1)	Part B: Miransertib PS (Cohort 2)
Number of subjects	17	22	1
Age Categorical Units: Participants			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous			
Standard deviation was not calculatable when n<2 for Part B Miransertib PS Cohort 2 arm			
Units: years			

arithmetic mean	8.2	9.9	12.0
standard deviation	± 9.9	± 6.7	± 9999

Gender Categorical Units: Participants			
Female	9	10	0
Male	8	12	1
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	3	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	5	0
White	17	13	1
More than one race	0	1	0
Unknown or Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic Or Latino	2	1	0
Not Hispanic Or Latino	15	20	1
Not Reported	0	1	0

Reporting group values	Part B: Miransertib PROS/PS (Cohort 3)	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)	Total
Number of subjects	8	2	50
Age Categorical Units: Participants			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous			
Standard deviation was not calculatable when n<2 for Part B Miransertib PS Cohort 2 arm			
Units: years arithmetic mean standard deviation	12.5 ± 9.1	20.0 ± 1.4	 -
Gender Categorical Units: Participants			
Female	3	1	23
Male	5	1	27
Race Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	1	0	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	6
White	6	2	39
More than one race	0	0	1
Unknown or Not Reported	0	0	0
Ethnicity Units: Subjects			
Hispanic Or Latino	0	0	3
Not Hispanic Or Latino	8	2	46
Not Reported	0	0	1

End points

End points reporting groups

Reporting group title	Part A: Miransertib PROS/PS

Reporting group description:

During Cycles 1-3, participants with either PROS (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha [PIK3CA]-related Overgrowth Spectrum) or PS (Proteus syndrome) received miransertib 15 mg/m^2 once daily (QD) (each cycle length = 28 days). From Cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 and then titrated to 35 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B: Miransertib PROS (Cohort 1)

Reporting group description:

During Cycles 1-3, participants with PROS who have a measurable lesion by volumetric magnetic resonance imaging (MRI) received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B: Miransertib PS (Cohort 2)

Reporting group description:

During Cycles 1-3, participants with PS who have a measurable lesion by standardized digital photography received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B: Miransertib PROS/PS (Cohort 3)

Reporting group description:

During Cycles 1-3, participants with PROS or PS who do not meet all the eligibility criteria for Cohorts 1 or 2 received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)

Reporting group description:

During cycles 1-48 (each cycle length = 28 days) or until disease progression, unacceptable toxicity, or discontinuation, participants previously treated with miransertib or currently receiving miransertib under Compassionate Use/Expanded Access continued to receive the current dose of miransertib (did not exceed 25 mg/m^2).

Primary: Number of Participants Who Experienced an Adverse Event (AE)

End point title	Number of Participants Who Experienced an Adverse Event (AE)[1]

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in a participant, whether or not considered drug related. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product and does not imply any judgment about causality. The analysis population included all participants who have received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Up to approximately 48 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: There was no statistical analysis planned for this endpoint.

End point values	Part A: Miransertib PROS/PS	Part B: Miransertib PROS (Cohort 1)	Part B: Miransertib PS (Cohort 2)	Part B: Miransertib PROS/PS (Cohort 3)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	22	1	8
Units: Participants	17	20	0	6

End point values	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Discontinued Study Treatment Due to an AE

End point title	Number of Participants Who Discontinued Study Treatment Due to an AE[2]

End point description:

An AE was defined as any untoward medical occurrence associated with the use of a drug in a participant, whether or not considered drug related. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product and does not imply any judgment about causality. The analysis population included all participants who have received at least one dose of study treatment.

End point type	Primary

End point timeframe:

Up to approximately 45 months

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: There was no statistical analysis planned for this endpoint.

End point values	Part A: Miransertib PROS/PS	Part B: Miransertib PROS (Cohort 1)	Part B: Miransertib PS (Cohort 2)	Part B: Miransertib PROS/PS (Cohort 3)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	22	1	8
Units: Participants	2	0	0	0

End point values	Part B:			

	Miransertib Compassionate Use/Expanded Access(Cohort 4)			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 48 months

Adverse event reporting additional description:

All cause mortality was reported on all enrolled participants and non-serious and serious AEs were reported on all participants who received at lease one dose of study treatment. Per protocol, disease progression (DP) was not considered an AE unless related to treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Part A: Miransertib PROS/PS

Reporting group description:

During Cycles 1-3, participants with either PROS (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha [PIK3CA]-related Overgrowth Spectrum) or PS (Proteus syndrome) received miransertib 15 mg/m^2 once daily (QD) (each cycle length = 28 days). From Cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 and then titrated to 35 mg/m^2 orally QD at the investigator’s discretion.

Reporting group title	Part B: Miransertib PROS (Cohort 1)

Reporting group description:

During Cycles 1-3, participants with PROS who have a measurable lesion by volumetric magnetic resonance imaging (MRI) received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B: Miransertib PS (Cohort 2)

Reporting group description:

During Cycles 1-3, participants with PS who have a measurable lesion by standardized digital photography received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B: Miransertib PROS/PS (Cohort 3)

Reporting group description:

During Cycles 1-3, participants with PROS or PS who do not meet all the eligibility criteria for Cohorts 1 or 2 received miransertib 15 mg/m^2 QD (each cycle length = 28 days). From cycles 4-48 or until disease progression, unacceptable toxicity, or discontinuation, participants received miransertib dose titrated to 25 mg/m^2 orally QD at the investigator's discretion.

Reporting group title	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)

Reporting group description:

During cycles 1-48 (each cycle length = 28 days) or until disease progression, unacceptable toxicity, or discontinuation, participants previously treated with miransertib or currently receiving miransertib under Compassionate Use/Expanded Access continued to receive the current dose of miransertib (did not exceed 25 mg/m^2).

Serious adverse events	Part A: Miransertib PROS/PS	Part B: Miransertib PROS (Cohort 1)	Part B: Miransertib PS (Cohort 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 17 (23.53%)	3 / 22 (13.64%)	0 / 1 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from	0	0	0

adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (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
Mouth haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (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
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (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	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (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			
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Serious adverse events	Part B: Miransertib PROS/PS (Cohort 3)	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (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			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (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	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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 A: Miransertib PROS/PS	Part B: Miransertib PROS (Cohort 1)	Part B: Miransertib PS (Cohort 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	18 / 22 (81.82%)	0 / 1 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Venous haemorrhage			

subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Lymphorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 17 (11.76%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	7	4	0
Inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Lithiasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Localised oedema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Mucosal inflammation			

subjects affected / exposed	3 / 17 (17.65%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	15 / 17 (88.24%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	74	3	0
Suprapubic pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Thirst			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Oedema genital			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Perineal erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Perineal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Testicular oedema			

subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	5	2	0
Vulvovaginal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Bradypnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	10 / 17 (58.82%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	17	4	0
Dysphonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Hiccups			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Laryngeal inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	1 / 17 (5.88%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	6	3	0
Nasal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			

subjects affected / exposed	3 / 17 (17.65%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	5	3	0
Pharyngeal erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tonsillolith			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract inflammation			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	5	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Anion gap			

subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Blood cholesterol increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Blood fibrinogen increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blood insulin increased			
subjects affected / exposed	2 / 17 (11.76%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	3	2	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Bone density decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fibrin D dimer decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fibrin D dimer increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Haematocrit increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haemoglobin increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Low density lipoprotein increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Lymphocyte count decreased			
subjects affected / exposed	2 / 17 (11.76%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	8	1	0
Lymphocyte count increased			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Monocyte count decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	4 / 17 (23.53%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	17	2	0
Neutrophil count increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	3 / 17 (17.65%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	5	1	0
Platelet count increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Urine ketone body present			

subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
White blood cell count decreased			
subjects affected / exposed	2 / 17 (11.76%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
White blood cell count increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Fall			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Head injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Wound dehiscence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			

Phimosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vascular malformation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	3	5	0
Headache			
subjects affected / exposed	3 / 17 (17.65%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	9	3	0
Paraesthesia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Petit mal epilepsy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Presyncope			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Sciatica			

subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 17 (11.76%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	4	3	0
Eosinophilia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Immune thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	2 / 17 (11.76%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Vertigo			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Eye disorders			

Conjunctival hyperaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Erythema of eyelid			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Eye discharge			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Eyelid oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 17 (41.18%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	11	5	0
Abdominal pain upper			
subjects affected / exposed	3 / 17 (17.65%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Aphthous ulcer			
subjects affected / exposed	4 / 17 (23.53%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	6 / 17 (35.29%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	20	1	0
Cheilitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	8 / 17 (47.06%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	12	3	0
Dental caries			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Dry mouth			

subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Food poisoning			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	4 / 22 (18.18%)	0 / 1 (0.00%)
occurrences (all)	1	6	0
Oral pain			
subjects affected / exposed	0 / 17 (0.00%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Salivary duct obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	5	1	0
Stomatitis			
subjects affected / exposed	2 / 17 (11.76%)	4 / 22 (18.18%)	0 / 1 (0.00%)
occurrences (all)	2	6	0
Swollen tongue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vomiting			

subjects affected / exposed	11 / 17 (64.71%)	5 / 22 (22.73%)	0 / 1 (0.00%)
occurrences (all)	24	13	0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Blister			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Bullous haemorrhagic dermatosis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Dermatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	1 / 17 (5.88%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Eczema			
subjects affected / exposed	2 / 17 (11.76%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	4	2	0
Perioral dermatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pityriasis rosea			

subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	2 / 17 (11.76%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	2	4	0
Rash maculo-papular			
subjects affected / exposed	5 / 17 (29.41%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	7	0	0
Skin disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin hypopigmentation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Skin lesion			
subjects affected / exposed	3 / 17 (17.65%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Skin mass			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Skin ulcer			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

Renal disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 17 (23.53%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	14	3	0
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Bone pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Osteochondrosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			

subjects affected / exposed	5 / 17 (29.41%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	27	4	0
Scoliosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)	4 / 22 (18.18%)	0 / 1 (0.00%)
occurrences (all)	2	10	0
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Coxsackie viral infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Cystitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Eye infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	4 / 17 (23.53%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	8	0	0
Impetigo			
subjects affected / exposed	3 / 17 (17.65%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	3	1	0

Infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 17 (17.65%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	4	0	0
Otitis media			
subjects affected / exposed	2 / 17 (11.76%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Otitis media acute			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	5 / 17 (29.41%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Pharyngotonsillitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	5 / 17 (29.41%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	6	0	0
Scarlet fever			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0

Soft tissue infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Tracheitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 17 (17.65%)	7 / 22 (31.82%)	0 / 1 (0.00%)
occurrences (all)	6	13	0
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Viraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	2 / 17 (11.76%)	3 / 22 (13.64%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Dehydration			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hyperinsulinaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			

subjects affected / exposed	2 / 17 (11.76%)	2 / 22 (9.09%)	0 / 1 (0.00%)
occurrences (all)	4	5	0
Hypermagnesaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 22 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	1 / 17 (5.88%)	1 / 22 (4.55%)	0 / 1 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	Part B: Miransertib PROS/PS (Cohort 3)	Part B:Miransertib Compassionate Use/Expanded Access(Cohort 4)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	1 / 1 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Venous haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Lymphorrhoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Face oedema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Lithiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Localised oedema			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Mucosal inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	8	0	
Suprapubic pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Thirst			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Oedema genital			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Perineal erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Perineal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Testicular oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Bradypnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	2 / 8 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	4	1	
Dysphonia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	7	0	
Hiccups			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Laryngeal inflammation			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Nasal obstruction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	2 / 8 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	2	1	
Pharyngeal erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Tachypnoea			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Tonsillolith			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Delirium			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Enuresis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Anion gap			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Blood bicarbonate decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Blood cholesterol increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood fibrinogen increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blood insulin increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	4 / 8 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	6	0	
Bone density decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
C-reactive protein increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Electrocardiogram QT prolonged			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Fibrin D dimer decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Fibrin D dimer increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Haematocrit increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Haemoglobin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Low density lipoprotein increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	4 / 8 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	10	0	
Lymphocyte count increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Monocyte count decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Neutrophil count increased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Platelet count decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Platelet count increased			

subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Urine ketone body present			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
White blood cell count decreased			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
White blood cell count increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Fall			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Head injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Scratch			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Wound dehiscence			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vascular malformation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Sinus bradycardia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Sinus tachycardia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Tachycardia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Headache			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Petit mal epilepsy			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Presyncope			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 8 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	6	0	
Eosinophilia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Immune thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Excessive cerumen production			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Ear pain			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Vertigo			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Conjunctival hyperaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Erythema of eyelid			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eye discharge			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eyelid oedema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 8 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	7	0	
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Aphthous ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Cheilitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			

subjects affected / exposed	4 / 8 (50.00%)	0 / 1 (0.00%)	
occurrences (all)	10	0	
Dental caries			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Food poisoning			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Frequent bowel movements			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Mouth haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Nausea			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	7	0	
Oral pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	4	0	
Salivary duct obstruction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Rectal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Swollen tongue			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	2 / 8 (25.00%)	1 / 1 (100.00%)	
occurrences (all)	6	1	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Blister			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Bullous haemorrhagic dermatosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Perioral dermatitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Petechiae			

subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Photosensitivity reaction			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Pityriasis rosea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Skin disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin hyperpigmentation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Skin hypopigmentation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Skin irritation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin mass			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Skin ulcer			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Proteinuria			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Renal disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Bone pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Flank pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Myalgia			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Osteochondrosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	3 / 8 (37.50%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Scoliosis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Spinal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Coxsackie viral infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Eye infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Fungal skin infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Impetigo			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Laryngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Otitis media acute			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Pharyngotonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	

Scarlet fever			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Soft tissue infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Tracheitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Viraemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 1 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	5	0	
Dehydration			

subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hyperinsulinaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Hypermagnesaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Hypocalcaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Hypophosphataemia			
subjects affected / exposed	2 / 8 (25.00%)	0 / 1 (0.00%)	
occurrences (all)	3	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 8 (12.50%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 February 2017	Major changes of Amendment (AM) 1 include modification to the definition of drug related toxicity to include any toxicities considered related, probably related, or possibly related to miransertib, updates to toxicities that prevent dose titrations, updates to dose limiting toxicity criteria for discontinuation of study treatment and modifications to the blood sample collection schedule for pharmacokinetic (PK) evaluation.
27 July 2017	Major changes of AM 2 include the possibility to open the miransertib capsule and administering it with a sweetened semiliquid, expanding window to collect overgrowth tissue, include blood sample collection for potential biomarkers during Cycle 1 Day 1 and removing fasting glucose requirements and electrocardiogram (ECG) for Cycle 1 Day 1 and expansion in contraception methods in accordance with clinical trials facilitation and coordination Group (CTFG) guidelines.
13 December 2017	Major changes of AM 3 include changing the eligibility criteria from 6 years to 2 years of age and removing phosphatase and tensin on chromosome 10 (PTEN) as an eligible mutation, adding of pain scale and to remove PK collection on Day 8, making biopsies optional, adding clarification that maximum dose titrations were not required if efficacy was seen at the lower dose levels and permitting intermittent use of high dose steroids as required.
20 September 2018	Major changes of AM 4 include updating inclusion criteria for participant population extending duration of treatment to 48 cycles and evaluating accumulated outcomes data, allowing surgical procedures as long as the procedures did not meet the discontinuation criteria, and increasing the enrollment number for participants in the study.
16 September 2019	Major changes of AM 6 include closing participant enrollment to Part A of the study, including Part B Cohort 4, updating study efficacy and exploratory endpoints, and increasing number of global sites.
08 October 2021	Major changes of AM 7 include removing all primary efficacy endpoints and all secondary endpoints, changing sponsor to ArQule, Inc (A Wholly owned subsidiary to Merch Sharp & Dohme, a subsidiary of Merck & Co., Inc), and updating primary objective to reflect safety and tolerability of miransertib.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
07 March 2022	Business reasons	-

Notes:

Limitations and caveats

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

Early termination due to business reasons

Notes: