Clinical trial results:
A Phase 2, Subprotocol of DAY101 Monotherapy for Patients With Recurrent, Progressive, or Refractory Solid Tumors With MAPK Pathway Aberrations

Summary

EudraCT number	2021-003768-29
Trial protocol	ES
Global end of trial date	08 July 2024

Results information

Result version number	v1 (current)
This version publication date	12 July 2025
First version publication date	12 July 2025

Trial information

Trial identification

Sponsor protocol code	DAY101-102a

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04985604
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Day One Biopharmaceuticals, Inc.
Sponsor organisation address	1800 Sierra Point Parkway, Suite 200, Brisbane, United States, 94005
Public contact	Study Director, Day One Biopharmaceuticals, Inc., 1-650-484-0899, clinicaltrials@dayonebio.com
Scientific contact	Study Director, Day One Biopharmaceuticals, Inc., 1-650-484-0899, clinicaltrials@dayonebio.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 July 2024
Global end of trial reached?	Yes
Global end of trial date	08 July 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objective:
• To determine the safety of DAY101 in combination with other therapies.
• To determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) of DAY101 in combination with other therapies.
• To evaluate the efficacy of DAY101 by RECIST version 1.1 or appropriate tumor response criteria as a monotherapy or in combination with other therapies

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 November 2021
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	Canada: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	United States: 8
Country: Number of subjects enrolled	Spain: 5
Worldwide total number of subjects	23
EEA total number of subjects	7

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 11 centers that enrolled subjects in 6 countries.

Pre-assignment

Screening details:

A total of 31 subjects consented, of which 23 subjects were enrolled into Melanoma and Tissue Agnostic cohorts. Remaining 8 subjects were screen failures.

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	Melanoma Cohort

Arm description:

Adult subjects (≥ 18 years) were administered Tovorafenib 600 mg orally (PO) once weekly (QW).

Arm type	Experimental
Investigational medicinal product name	Tovorafenib
Investigational medicinal product code	
Other name	DAY101
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tovorafenib tablet for oral use.

Arm title	Tissue Agnostic Cohort

Arm description:

Adult subjects (≥ 18 years) were administered Tovorafenib 600 mg PO QW.

Arm type	Experimental
Investigational medicinal product name	Tovorafenib
Investigational medicinal product code	
Other name	DAY101
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Tovorafenib tablet for oral use.

Number of subjects in period 1	Melanoma Cohort	Tissue Agnostic Cohort
Started	8	15
Completed	4	8
Not completed	4	7
Consent withdrawn by subject	-	1

Death	4	6

Baseline characteristics

Reporting groups	
Reporting group title	Melanoma Cohort
Reporting group description:	
Adult subjects (≥ 18 years) were administered Tovorafenib 600 mg orally (PO) once weekly (QW).	
Reporting group title	Tissue Agnostic Cohort
Reporting group description:	
Adult subjects (≥ 18 years) were administered Tovorafenib 600 mg PO QW.	

Reporting group values	Melanoma Cohort	Tissue Agnostic Cohort	Total
Number of subjects	8	15	23
Age categorical Units: Subjects			
Adults (18-64 years)	7	13	20
From 65-84 years	1	2	3
Age continuous Units: years			
median	58.0	45.0	
full range (min-max)	26 to 71	21 to 71	-
Gender categorical Units: Subjects			
Female	4	7	11
Male	4	8	12

End points

End points reporting groups

Reporting group title	Melanoma Cohort
Reporting group description:	
Adult subjects (≥ 18 years) were administered Tovorafenib 600 mg orally (PO) once weekly (QW).	
Reporting group title	Tissue Agnostic Cohort
Reporting group description:	
Adult subjects (≥ 18 years) were administered Tovorafenib 600 mg PO QW.	

Primary: Overall Response Rate (ORR) by the Investigator

End point title	Overall Response Rate (ORR) by the Investigator[1]

End point description:

ORR was defined as the percentage of participants with the best overall confirmed response of complete response (CR) or partial response (PR) according to the appropriate response assessment criteria including Response Evaluation Criteria in Solid Tumors (RECIST 1.1) or Response Assessment in Neuro-Oncology (RANO) for the disease setting as assessed by the Investigator. CR or PR was confirmed at a subsequent scan (>=4 weeks) if the criteria for each are met. The exact 95% confidence intervals (CIs) were calculated using Clopper-Pearson method. Efficacy Analysis Set comprises of all participants who received at least one dose of study drug and have measurable disease as determined by the Investigator at baseline.

End point type	Primary

End point timeframe:

Up to 23 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 statistical analysis was performed for this endpoint.

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: percentage of participants				
number (confidence interval 95%)	50.0 (15.7 to 84.3)	40.0 (16.3 to 67.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to study intervention. A serious adverse event (SAE) is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing

hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect or any other situation according to medical or scientific judgment. An AE is considered to be treatment-emergent if it has a start date/time on or after first administration of study drug until 30 days after last dose of study drug and before the start of subsequent therapy, whichever comes earlier. The distribution of AEs was analyzed by the type, frequency and severity for TEAEs. Safety Analysis Set has of all patients enrolled in the study who receive at least one dose of study drug.

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: Participants				
number (not applicable)				
Any TEAE	8	15		
TEAEs Related to Study Drug	8	13		
Any serious TEAE	2	8		
Serious TEAEs Related to Study Drug	0	1		
TEAEs with Severity Grade 3 or Higher	5	8		
TEAEs Related to Study Drug with Severity Grade 3	2	3		
TEAEs Leading to Death	0	0		
TEAEs Related to Study Drug Leading to Death	0	0		
TEAEs Leading to Study Drug Discontinuation	1	0		
EAEs Related to Study Drug Leading to Study Drug D	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Worst Case Hematology Results by Maximum Grade Increase Post-baseline Relative to Baseline

End point title	Number of Participants With Worst Case Hematology Results by Maximum Grade Increase Post-baseline Relative to Baseline

End point description:

Blood samples were collected for the analysis of following hematology parameters: anemia, neutrophil count decreased and white blood cell decreased. Grade 1 (G1): mild; Grade 2 (G2): moderate; Grade 3 (G3): severe; Grade 4 (G4) life-threatening or disabling. Higher grade indicates greater severity and an increase in Common Terminology Criteria for Adverse Events (CTCAE) grade was defined relative to the Baseline grade. Any worst-case post baseline increase to G2, G3, and G4 are presented. The laboratory parameters were graded according to CTCAE version 5.

End point type	Secondary

End point timeframe:

Baseline and up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: Participants				
number (not applicable)				
Anemia, Increased to Grade 2	3	5		
Anemia, Increased to Grade 3	2	2		
Anemia, Increased to Grade 4	0	0		
Neutrophil count decreased, Increased to Grade 2	0	2		
Neutrophil count decreased, Increased to Grade 3	0	1		
Neutrophil count decreased, Increased to Grade 4	0	0		
White blood cell decreased, Increased to Grade 2	0	2		
White blood cell decreased, Increased to Grade 3	0	0		
White blood cell decreased, Increased to Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Worst Case Chemistry Results by Maximum Grade Increase Post-baseline Relative to Baseline

End point title	Number of Participants With Worst Case Chemistry Results by Maximum Grade Increase Post-baseline Relative to Baseline

End point description:

Blood samples were collected for the analysis of following chemistry parameters: creatine phosphokinase (CPK) increased, hypokalemia, hypoalbuminemia, hypercalcemia, hypocalcemia and hyponatremia. Grade 1 (G1): mild; Grade 2 (G2): moderate; Grade 3 (G3): severe; Grade 4 (G4) life-threatening or disabling. Higher grade indicates greater severity and an increase in CTCAE grade was defined relative to the Baseline grade. Any worst-case post baseline increases to G2, G3, and G4 are presented. The laboratory parameters were graded according to CTCAE version 5. Safety Analysis Set comprises of all patients enrolled in the study who receive at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline and up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: Participants				
number (not applicable)				
CPK increased, Increased to Grade 2	2	4		
CPK increased, Increased to Grade 3	0	1		
CPK increased, Increased to Grade 4	1	0		
Hypoalbuminemia, Increased Grade 2	1	2		
Hypoalbuminemia, Increased Grade 3	0	0		
Hypoalbuminemia, Increased Grade 4	0	0		
Hypokalemia, Increased to Grade 2	1	5		
Hypokalemia, Increased to Grade 3	0	1		
Hypokalemia, Increased to Grade 4	0	0		
Hyponatremia, Increased to Grade 2	1	1		
Hyponatremia, Increased to Grade 3	0	0		
Hyponatremia, Increased to Grade 4	0	0		
Hypercalcemia, Increased to Grade 2	0	0		
Hypercalcemia, Increased to Grade 3	0	1		
Hypercalcemia, Increased to Grade 4	0	0		
Hypocalcemia, Increased to Grade 2	0	1		
Hypocalcemia, Increased to Grade 3	0	0		
Hypocalcemia, Increased to Grade 4	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) in Participants With Best Overall Response

End point title	Duration of Response (DOR) in Participants With Best Overall Response

End point description:

Duration of response was defined as the interval from the date of the first documentation of tumor response (CR or PR) that was subsequently confirmed by investigator assessment to the date of first occurrence of radiographic disease progression based on RECIST 1.1 or RANO criteria or death due to any cause, whichever occurs earlier. DOR was estimated using Kaplan-Meier method. Participants in the Efficacy Analysis Set who have a confirmed response of CR or PR. 99999 indicates the data and very small number of participants did not allow meaningful calculation of the upper limit of 95% Confidence Interval.

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: Months				
median (confidence interval 95%)	5.6 (3.0 to 99999)	9.2 (3.5 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Progression Free Survival

End point title	Duration of Progression Free Survival

End point description:

Progression free survival was defined as the interval from the date of the first dose to the first occurrence of radiographic disease progression based on RECIST 1.1 or RANO criteria or death due to any cause, whichever occurs earlier. Progression free survival was estimated using Kaplan-Meier method. 99999 indicates the data and very small number of participants did not allow meaningful calculation of the upper limit of 95% Confidence Interval.

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: Months				
median (confidence interval 95%)	5.5 (1.8 to 12.5)	5.5 (1.7 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Survival

End point title	Duration of Overall Survival

End point description:

Overall survival is defined as the interval from the date of the first dose until the recorded date of death due to any cause. Overall survival was estimated using Kaplan-Meier method. 99999 indicates the data and very small number of participants did not allow meaningful calculation of the upper limit of 95% Confidence Interval. 88888 indicates the median Overall Survival was not reached, and the data did not allow meaningful calculation of the upper limit of median and 95% Confidence Interval.

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	15		
Units: Months				
median (confidence interval 95%)	18.9 (3.4 to 99999)	88888 (5.5 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

Time to Response was defined in participants with best overall response of complete response or partial response as determined by Investigator. It is the interval from the date of the first dose to date of first documentation of tumor response that was subsequently confirmed by investigator assessment.

End point type	Secondary

End point timeframe:

Up to 23 months

End point values	Melanoma Cohort	Tissue Agnostic Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	6		
Units: Months				
median (confidence interval 95%)	1.76 (1.66 to 6.44)	1.82 (1.77 to 1.87)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 23 months

Adverse event reporting additional description:

TEAEs and serious TEAEs were analyzed in Safety Analysis Set which comprised of all subjects enrolled in the study who received at least one dose of tovorafenib.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Melanoma Cohort

Reporting group description:

Adult participants (≥ 18 years) were administered Tovorafenib 600 mg orally (PO) once weekly (QW).

Reporting group title	Tissue Agnostic Cohort

Reporting group description:

Adult participants (≥ 18 years) were administered Tovorafenib 600 mg PO QW.

Serious adverse events	Melanoma Cohort	Tissue Agnostic Cohort	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	8 / 15 (53.33%)	
number of deaths (all causes)	2	4	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lung			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour associated fever			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemorrhage intracranial			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Melanoma Cohort	Tissue Agnostic Cohort	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	15 / 15 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 8 (25.00%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Melanocytic naevus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

Metastases to lung			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Orthostatic hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	3 / 8 (37.50%)	2 / 15 (13.33%)	
occurrences (all)	3	2	
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	4	
Fatigue			
subjects affected / exposed	4 / 8 (50.00%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Oedema			
subjects affected / exposed	1 / 8 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Chills			

subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gait disturbance			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Generalised oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Mucosal inflammation			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	3 / 15 (20.00%)	
occurrences (all)	2	3	
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Epistaxis			
subjects affected / exposed	1 / 8 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hypoxia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Productive cough			

subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pulmonary hypertension			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Insomnia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 8 (12.50%)	5 / 15 (33.33%)	
occurrences (all)	3	6	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 8 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Weight decreased			
subjects affected / exposed	2 / 8 (25.00%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Blood bilirubin increased			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood calcium decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood magnesium decreased			

subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood phosphorus decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tri-iodothyronine increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Troponin I increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Lip injury			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Tooth fracture			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pericardial effusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Sinus tachycardia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 8 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Headache			
subjects affected / exposed	2 / 8 (25.00%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Dizziness			

subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dysarthria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Pyramidal tract syndrome			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 8 (62.50%)	7 / 15 (46.67%)	
occurrences (all)	6	8	
Eosinophilia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eye disorders			
Retinal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Vision blurred			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Blepharitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Conjunctivitis allergic			

subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eye disorder			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Eye pruritus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Periorbital oedema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Visual acuity reduced			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vitreous detachment			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vitreous floaters			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 8 (37.50%)	3 / 15 (20.00%)	
occurrences (all)	3	3	
Vomiting			
subjects affected / exposed	1 / 8 (12.50%)	4 / 15 (26.67%)	
occurrences (all)	1	4	
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	

Nausea			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	3	
Oral pain			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Anal haemorrhage			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Haematemesis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 8 (37.50%)	4 / 15 (26.67%)	
occurrences (all)	3	5	
Rash			
subjects affected / exposed	3 / 8 (37.50%)	3 / 15 (20.00%)	
occurrences (all)	3	3	
Dermatitis acneiform			
subjects affected / exposed	1 / 8 (12.50%)	4 / 15 (26.67%)	
occurrences (all)	1	4	
Hair colour changes			
subjects affected / exposed	0 / 8 (0.00%)	4 / 15 (26.67%)	
occurrences (all)	0	4	
Rash maculo-papular			

subjects affected / exposed	2 / 8 (25.00%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	3	
Acne			
subjects affected / exposed	1 / 8 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Photosensitivity reaction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Pigmentation disorder			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Rash erythematous			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vitiligo			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	1 / 8 (12.50%)	6 / 15 (40.00%)	
occurrences (all)	1	6	
Neck pain			
subjects affected / exposed	1 / 8 (12.50%)	2 / 15 (13.33%)	
occurrences (all)	1	2	
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Back pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Herpes zoster			

subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 8 (25.00%)	2 / 15 (13.33%)	
occurrences (all)	2	2	
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	3 / 15 (20.00%)	
occurrences (all)	0	4	
Hypophosphataemia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Hypercalcaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyperchloraemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 September 2021	• Extended inclusion criteria on archival tissue window. • Updated exclusion criteria on QTc threshold from >450 milliseconds (ms) to >470 ms. • Revised contraceptive guidance and collection of pregnancy information. • Added Lansky Performance Score assessment. • Added CRAF/RAF1 fusions and CRAF/RAF1 amplifications to acceptable genomic alterations. • Added stopping criteria. • Added visual symptom assessment, updated ophthalmologic exam assessment timepoints. • Clarified vital sign collection timepoints.
19 October 2021	• Removed sentence: Participants ages 12 up to < 18 years will be included in the study provided their BSA is ≥ 1.5 m^2. Updated study design schema. • Revised end of study to reflect approximately 25 months after last participant is enrolled. Per Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) request, revised inclusion criterion definition of standard-of-care treatments. • Per ANSM request, exclusion criteria regarding potential for QT prolongation have been revised, participants with uveal melanoma to be excluded, included regular neurologic examinations for participants with CNS tumors who enroll in the Tissue Agnostic Cohort, modified protocol to add requested triplicate ECGs. • Clarified definition of standard-of-care treatment to include locally directed therapy, such as surgery or radiotherapy. • Added results from Study FIREFLY-1/PNOC026 and Study PNOC014. Per ANSM request, added dose modification guidelines for edema-associated AEs, revised guidance for retinal detachment, revised course of action in the case of a Grade 4 rash recurrence, added guidance on wearing sunglasses and increased SPF to ≥50, clarified course of action if second occurrence of increase CPK occurs. • Per PCL-Canada recommendations, revised section to include bilirubin assessment guidance. • Per ANSM recommendations, revised definition of Grade 3 increased liver transaminases. Also clarified course of action in the case of Grade 3 or 4 LFT elevation and added QTc prolongation guidance. • Per ANSM request, modified concomitant medications. Added palliative radiotherapy. Clarified concomitant medications and recommendation of prohibited concomitant medications. Addition of Tanner Stage. • Per ANSM recommendation, added neurological examinations more frequently for participants with neurological tumors. • Added Adverse Events of Special Interest guidance. • Established Independent Data Monitoring Committee.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
08 July 2024	The study was terminated at Sponsor's discretion.	-

Notes:

Limitations and caveats

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

DAY101-102b sub-study is a phase1/2 clinical trial, however, it was terminated due to sponsor decision after completion of phase 1 dose escalation and study did not progress to phase 2 dose-expansion portion. Hence results for 102b will not be posted

Notes: