Clinical trial results:
A Phase III, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of alpelisib (BYL719) in combination with nab-paclitaxel in patients with advanced triple negative breast cancer with either phosphoinositide-3-kinase catalytic subunit alpha (PIK3CA) mutation or phosphatase and tensin homolog protein (PTEN) loss without PIK3CA mutation

Summary

EudraCT number	2019-002637-11
Trial protocol	HU FR SK DE GB IT NO AT BG SI PL HR GR RO PT
Global end of trial date	05 February 2026

Results information

Result version number	v1 (current)
This version publication date	29 October 2026
First version publication date	29 October 2026

Trial information

Trial identification

Sponsor protocol code	CBYL719H12301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04251533
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Lichtstrasse 35, Basel, Switzerland, 4056
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	05 February 2026
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 February 2026
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to determine whether treatment with alpelisib in combination with nab-paclitaxel is safe and effective in subjects with advanced triple negative breast cancer (aTNBC) who carry either a PIK3CA mutation (Study Part A) or have PTEN loss (Study Part B1) or PTEN loss without PIK3CA mutation (Study Part B2)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 June 2020
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	Argentina: 5
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	China: 19
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Croatia: 1
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	India: 5
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Malaysia: 14
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Peru: 2

Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Slovenia: 1
Country: Number of subjects enrolled	South Africa: 2
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Türkiye: 8
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 6
Worldwide total number of subjects	137
EEA total number of subjects	39

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)	104
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 137 participants were enrolled from 30 countries across Europe, Asia-Pacific, North America, South America, and Africa.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: alpelisib + nab-paclitaxel

Arm description:

Participants received alpelisib 300 mg orally in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.

Arm type	Experimental
Investigational medicinal product name	nab-paclitaxel
Investigational medicinal product code	
Other name	abraxane
Pharmaceutical forms	Powder for suspension for injection, Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle

Investigational medicinal product name	alpelisib
Investigational medicinal product code	
Other name	BYL719
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg orally, once per day (QD), tablets

Arm title	Part A: placebo + nab-paclitaxel

Arm description:

Participants received placebo in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.

Arm type	Placebo
Investigational medicinal product name	nab-paclitaxel
Investigational medicinal product code	
Other name	abraxane
Pharmaceutical forms	Powder for suspension for injection, Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle

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

Dosage and administration details:

300 mg orally, once per day (QD), tablets

Arm title	Part B1: alpelisib + nab-paclitaxel

Arm description:

Participants received alpelisib 300 mg administered orally in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.

Arm type	Experimental
Investigational medicinal product name	nab-paclitaxel
Investigational medicinal product code	
Other name	abraxane
Pharmaceutical forms	Powder for suspension for injection, Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle

Investigational medicinal product name	alpelisib
Investigational medicinal product code	
Other name	BYL719
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg orally, once per day (QD), tablets

Number of subjects in period 1	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel	Part B1: alpelisib + nab-paclitaxel
Started	52	50	35
Completed	0	0	0
Not completed	52	50	35
Adverse event, serious fatal	6	1	3
Physician decision	3	5	5
Subject decision	1	4	1
Adverse event, non-fatal	2	2	1
Study terminated by sponsor	-	2	-
Progressive disease	40	36	25

Baseline characteristics

Reporting groups	
Reporting group title	Part A: alpelisib + nab-paclitaxel
Reporting group description:	
Participants received alpelisib 300 mg orally in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.	
Reporting group title	Part A: placebo + nab-paclitaxel
Reporting group description:	
Participants received placebo in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.	
Reporting group title	Part B1: alpelisib + nab-paclitaxel
Reporting group description:	
Participants received alpelisib 300 mg administered orally in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.	

Reporting group values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel	Part B1: alpelisib + nab-paclitaxel
Number of subjects	52	50	35
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	32	30
From 65-84 years	10	18	5
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	56.8	59.1	48.4
standard deviation	± 9.76	± 11.34	± 12.21
Sex: Female, Male Units: participants			
Female	52	49	35
Male	0	1	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	17	19	10
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	32	30	23
More than one race	1	1	0
Unknown or Not Reported	1	0	0

Reporting group values	Total		
Number of subjects	137		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	104		
From 65-84 years	33		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	136		
Male	1		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	46		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	85		
More than one race	2		
Unknown or Not Reported	1		

End points

End points reporting groups

Reporting group title	Part A: alpelisib + nab-paclitaxel
Reporting group description:	
Participants received alpelisib 300 mg orally in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.	
Reporting group title	Part A: placebo + nab-paclitaxel
Reporting group description:	
Participants received placebo in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.	
Reporting group title	Part B1: alpelisib + nab-paclitaxel
Reporting group description:	
Participants received alpelisib 300 mg administered orally in combination with nab-paclitaxel 100 mg/m² administered intravenously on Days 1, 8, and 15 of each 28-day treatment cycle.	

Primary: Progression-free Survival (PFS) Per Investigator Assessment in Study Part A

End point title	Progression-free Survival (PFS) Per Investigator Assessment in Study Part A[1]
End point description:	
PFS was defined as time from the date of randomization to the date of the first documented progressive disease (PD) or death due to any cause. PFS was assessed via a local radiology assessment according to RECIST 1.1. PD = At least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm^2. PFS was censored at the date of the last adequate tumor assessment, if no PFS event was observed prior to the analysis cut-off date.	
End point type	Primary
End point timeframe:	
Once all participants have completed at least 6 months of study treatment or have discontinued from study treatment, up to 35 months	
Notes:	
[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Endpoint only applicable to Study Part A	

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	50		
Units: months				
median (confidence interval 95%)	7.2 (3.71 to 8.57)	5.6 (3.75 to 12.68)		

Statistical analyses

Statistical analysis title	PFS in Study Part A
Comparison groups	Part A: alpelisib + nab-paclitaxel v Part A: placebo + nab-paclitaxel

Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	2.41

Primary: Overall Response Rate (ORR) Based on Local Radiology Assessments in Participants with Measurable Disease at Baseline in Study Part B1

End point title	Overall Response Rate (ORR) Based on Local Radiology Assessments in Participants with Measurable Disease at Baseline in Study Part B1[2][3]

End point description:

ORR was defined as the percentage of participants with best overall response (BOR) of confirmed complete response (CR) or confirmed partial response (PR) according to RECIST 1.1. BOR was defined as the best response recorded from the start of the study treatment until progressive disease (PD)/recurrence. CR = Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm. PR = At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters; PD = At least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm^2.

End point type	Primary

End point timeframe:

Up to 6 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: Only Descriptive analysis performed

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part B1

End point values	Part B1: alpelisib + nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage of participants				
number (confidence interval 95%)	14.3 (4.8 to 30.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival in Study Part A

End point title	Overall Survival in Study Part A[4]

End point description:

Overall survival (OS) was defined as the time from the date of randomization to the date of death due to any cause. If a participant was not known to have died, OS was censored at the latest date the participant was known to be alive (on or before the cut-off date), i.e., the last known date the participant was alive (last contact date).

End point type	Secondary

End point timeframe:

Up to 68 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part A

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	50[5]		
Units: Months				
median (confidence interval 95%)	14.9 (10.68 to 23.49)	27.6 (10.22 to 999)		

Notes:

[5] - 95% CI upper limit not estimable due to insufficient events.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) with Confirmed Response in Study Part A

End point title	Overall Response Rate (ORR) with Confirmed Response in Study Part A[6]

End point description:

ORR with confirmed response was the percentage of participants with best overall response (BOR) of confirmed complete response (CR) or confirmed partial response (PR), as per local review and according to RECIST 1.1. BOR was defined as the best response recorded from the start of the study treatment until progressive disease (PD)/recurrence. CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm. PR= At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters; PD= At least a 20% increase in the sum of diameters of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition, the sum must also demonstrate an absolute increase of at least 5 mm.

End point type	Secondary

End point timeframe:

Once all participants have completed at least 6 months of study treatment or have discontinued from study treatment, up to 35 months

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part A

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	50		
Units: percentage of participants				
number (confidence interval 95%)	40.4 (27.0 to 54.9)	34.0 (21.2 to 48.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) with Confirmed Response in Study Part A

End point title	Clinical Benefit Rate (CBR) with Confirmed Response in Study Part A[7]

End point description:

Clinical benefit rate (CBR) was defined as the percentage of participants with a best overall response of complete response (CR), or partial response (PR) or an overall lesion response of stable disease (SD), lasting as per local review, for a duration of at least 24 weeks. CR, PR and SD are defined according to RECIST 1.1 based on investigator's assessment. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary

End point timeframe:

Once all participants have completed at least 6 months of study treatment or have discontinued from study treatment, up to 35 months

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part A

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	50		
Units: percentage of participants				
number (confidence interval 95%)	50.0 (35.8 to 64.2)	44.0 (30.0 to 58.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) with Confirmed Response in Study Part B1

End point title	Clinical Benefit Rate (CBR) with Confirmed Response in Study Part B1[8]

End point description:

Clinical benefit rate (CBR) was defined as the percentage of participants with a best overall response of

complete response (CR), or partial response (PR) or an overall lesion response of stable disease (SD), lasting as per local review, for a duration of at least 24 weeks. CR, PR and SD are defined according to RECIST 1.1 based on investigator's assessment. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters. SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

End point type	Secondary

End point timeframe:

Up to 6 months

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part B1

End point values	Part B1: alpelisib + nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: percentage of participants				
number (confidence interval 95%)	25.7 (12.5 to 43.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) in Study Part A

End point title	Time to Response (TTR) in Study Part A[9]

End point description:

Time to response (TTR) was defined as the time from the date of randomization/enrolment to the first documented response of either complete response (CR) or partial response (PR), which must be subsequently confirmed (although date of initial response is used, not date of confirmation). CR and PR were based on tumor response data as per local review and according to RECIST 1.1.
CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Once all participants have completed at least 6 months of study treatment or have discontinued from study treatment, up to 35 months

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part A

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52[10]	50[11]		
Units: months				
median (confidence interval 95%)	999 (4.14 to 999)	999 (999 to 999)		

Notes:

[10] - Median and upper 95% CI limit not estimable due to insufficient number of events.

[11] - Median and 95% CI limits were not estimable due to an insufficient number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) in Study Part B1

End point title	Time to Response (TTR) in Study Part B1[12]

End point description:

Time to response (TTR) was defined as the time from the date of randomization/enrolment to the first documented response of either complete response (CR) or partial response (PR), which must be subsequently confirmed (although date of initial response was used, not date of confirmation). CR and PR were based on tumor response data as per local review and according to RECIST 1.1. CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Up to 6 months

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part B1

End point values	Part B1: alpelisib + nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	35[13]			
Units: months				
median (confidence interval 95%)	999 (999 to 999)			

Notes:

[13] - Median and 95% CI limits were not estimable due to an insufficient number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) with Confirmed Response in Study Part A

End point title	Duration of Response (DOR) with Confirmed Response in Study Part A[14]

End point description:

Duration of response (DOR) with confirmed response only applied to participants whose best overall response (BOR) was confirmed complete response (CR) or confirmed partial response (PR) according to RECIST 1.1 based on tumor response data per local review. The start date was the date of first documented response of CR or PR (i.e. the start date of response, not the date when response was confirmed), and the end date was defined as the date of the first documented progressive disease (PD) or death due to underlying cancer. CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the

baseline sum of diameters.

End point type	Secondary

End point timeframe:

Once all participants have completed at least 6 months of study treatment or have discontinued from study treatment, up to 35 months

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part A

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	17[15]		
Units: months				
median (confidence interval 95%)	7.39 (5.59 to 9.53)	999 (10.55 to 999)		

Notes:

[15] - Median and upper 95% CI limit not estimable due to insufficient number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) with Confirmed Response in Study Part B1

End point title	Duration of Response (DOR) with Confirmed Response in Study Part B1[16]

End point description:

Duration of response (DOR) with confirmed response only applied to participants whose best overall response (BOR) was confirmed complete response (CR) or confirmed partial response (PR) according to RECIST 1.1 based on tumor response data per local review. The start date was the date of first documented response of CR or PR (i.e. the start date of response, not the date when response was confirmed), and the end date was defined as the date of the first documented progressive disease (PD) or death due to underlying cancer. CR=Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to < 10 mm; PR= At least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Up to approximately 20 months

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part B1

End point values	Part B1: alpelisib + nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	5[17]			
Units: months				
median (confidence interval 95%)	11.04 (7.46 to 999)			

Notes:

[17] - Upper 95% CI limit not estimable due to insufficient number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS) Per Investigator Assessment in Study Part B1

End point title	Progression-free Survival (PFS) Per Investigator Assessment in Study Part B1[18]

End point description:

PFS was defined as time from the date of enrolment to the date of the first documented progressive disease (PD) or death due to any cause. PFS was assessed via a local radiology assessment according to RECIST 1.1. PD=At least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm^2. PFS was censored at the date of the last adequate tumor assessment, if no PFS event was observed prior to the analysis cut-off date.

End point type	Secondary

End point timeframe:

Up to 6 months

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part B1

End point values	Part B1: alpelisib + nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: months				
median (confidence interval 95%)	3.71 (3.15 to 5.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival in Study Part B1

End point title	Overall Survival in Study Part B1[19]

End point description:

Overall survival for Part B1 was defined as the number of participants who were alive at the end of the post-treatment period.

End point type	Secondary

End point timeframe:

Up to approximately 68 months.

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part B1

End point values	Part B1: alpelisib + nab-paclitaxel			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Participants	21			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS Based on Local Radiology Assessments Using RECIST 1.1 Criteria for Participants by PIK3CA Mutation Status Measured in Baseline Circulating Tumor Deoxyribonucleic Acid (ctDNA) in Study Part A

End point title	PFS Based on Local Radiology Assessments Using RECIST 1.1 Criteria for Participants by PIK3CA Mutation Status Measured in Baseline Circulating Tumor Deoxyribonucleic Acid (ctDNA) in Study Part A[20]

End point description:

PFS in participants with PIK3CA mutation as measured in ctDNA. PFS was defined as time from the date of randomization to the date of the first documented progression or death due to any cause.

End point type	Secondary

End point timeframe:

Once all participants have completed at least 6 months of study treatment or have discontinued from study treatment, up to 35 months

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint only applicable to Study Part A

End point values	Part A: alpelisib + nab-paclitaxel	Part A: placebo + nab-paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	22		
Units: months				
median (confidence interval 95%)	7.5 (3.58 to 9.17)	3.5 (1.77 to 5.85)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from first dose until 30 days after last dose, for up to 28 months (Part A: alpelisib+nab-paclitaxel), 58 months (Part A: placebo+nab-paclitaxel), and 31 months (Part B1: alpelisib+nab-paclitaxel).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Placebo + Nab Part A
Reporting group description:	
Placebo + Nab Part A	
Reporting group title	Alpelisib + Nab Part A
Reporting group description:	
Alpelisib + Nab Part A	
Reporting group title	Alpelisib + Nab Part B1
Reporting group description:	
Alpelisib + Nab Part B1	

Serious adverse events	Placebo + Nab Part A	Alpelisib + Nab Part A	Alpelisib + Nab Part B1
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 50 (34.00%)	24 / 52 (46.15%)	14 / 35 (40.00%)
number of deaths (all causes)	6	7	3
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Infected neoplasm			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 50 (2.00%)	2 / 52 (3.85%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 50 (4.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial fistula			

subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrothorax			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 50 (2.00%)	5 / 52 (9.62%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	10 / 10	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	2 / 50 (4.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocyte count decreased			

subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Diabetic neuropathy			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 50 (2.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	2 / 2	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis haemorrhagic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 50 (0.00%)	3 / 52 (5.77%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	8 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 50 (2.00%)	2 / 52 (3.85%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	4 / 4	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neck pain			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess soft tissue			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Device related infection			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			

subjects affected / exposed	1 / 50 (2.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Breast abscess			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 50 (2.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	3 / 52 (5.77%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	6 / 6	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Postoperative wound infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 50 (0.00%)	3 / 52 (5.77%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo + Nab Part A	Alpelisib + Nab Part A	Alpelisib + Nab Part B1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 50 (94.00%)	51 / 52 (98.08%)	35 / 35 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 50 (4.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	4	4	6
Lymphoedema			
subjects affected / exposed	1 / 50 (2.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	2	4	6
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 50 (0.00%)	3 / 52 (5.77%)	0 / 35 (0.00%)
occurrences (all)	0	6	0
Asthenia			
subjects affected / exposed	5 / 50 (10.00%)	9 / 52 (17.31%)	4 / 35 (11.43%)
occurrences (all)	12	20	10
Fatigue			
subjects affected / exposed	12 / 50 (24.00%)	13 / 52 (25.00%)	9 / 35 (25.71%)
occurrences (all)	40	32	22
Malaise			
subjects affected / exposed	0 / 50 (0.00%)	3 / 52 (5.77%)	1 / 35 (2.86%)
occurrences (all)	0	6	2
Peripheral swelling			
subjects affected / exposed	3 / 50 (6.00%)	3 / 52 (5.77%)	2 / 35 (5.71%)
occurrences (all)	6	6	4
Pain			
subjects affected / exposed	2 / 50 (4.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	4	4	4
Oedema peripheral			
subjects affected / exposed	9 / 50 (18.00%)	4 / 52 (7.69%)	5 / 35 (14.29%)
occurrences (all)	22	8	16
Mucosal inflammation			
subjects affected / exposed	2 / 50 (4.00%)	5 / 52 (9.62%)	3 / 35 (8.57%)
occurrences (all)	6	14	12
Pyrexia			

subjects affected / exposed	5 / 50 (10.00%)	8 / 52 (15.38%)	5 / 35 (14.29%)
occurrences (all)	14	20	20
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 50 (4.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	4	0	4
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	4 / 50 (8.00%)	3 / 52 (5.77%)	0 / 35 (0.00%)
occurrences (all)	8	6	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 50 (14.00%)	9 / 52 (17.31%)	5 / 35 (14.29%)
occurrences (all)	24	22	10
Dyspnoea			
subjects affected / exposed	3 / 50 (6.00%)	5 / 52 (9.62%)	5 / 35 (14.29%)
occurrences (all)	6	14	10
Pleural effusion			
subjects affected / exposed	1 / 50 (2.00%)	2 / 52 (3.85%)	5 / 35 (14.29%)
occurrences (all)	2	4	10
Oropharyngeal pain			
subjects affected / exposed	2 / 50 (4.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	4	6	4
Productive cough			
subjects affected / exposed	1 / 50 (2.00%)	5 / 52 (9.62%)	1 / 35 (2.86%)
occurrences (all)	2	10	2
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 50 (6.00%)	0 / 52 (0.00%)	0 / 35 (0.00%)
occurrences (all)	6	0	0
Insomnia			
subjects affected / exposed	6 / 50 (12.00%)	3 / 52 (5.77%)	2 / 35 (5.71%)
occurrences (all)	14	6	4
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	3 / 50 (6.00%)	7 / 52 (13.46%)	4 / 35 (11.43%)
occurrences (all)	6	24	8
Alpha hydroxybutyrate dehydrogenase increased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	4
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 50 (6.00%)	3 / 52 (5.77%)	3 / 35 (8.57%)
occurrences (all)	6	6	12
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 50 (16.00%)	9 / 52 (17.31%)	4 / 35 (11.43%)
occurrences (all)	22	30	8
Blood chloride decreased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	4
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 50 (0.00%)	2 / 52 (3.85%)	4 / 35 (11.43%)
occurrences (all)	0	4	10
Blood insulin increased			
subjects affected / exposed	3 / 50 (6.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences (all)	8	2	2
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 50 (2.00%)	4 / 52 (7.69%)	1 / 35 (2.86%)
occurrences (all)	2	20	4
Blood creatinine increased			
subjects affected / exposed	1 / 50 (2.00%)	6 / 52 (11.54%)	4 / 35 (11.43%)
occurrences (all)	4	36	10
Gamma-glutamyltransferase increased			
subjects affected / exposed	9 / 50 (18.00%)	10 / 52 (19.23%)	4 / 35 (11.43%)
occurrences (all)	20	22	10
Lipase increased			
subjects affected / exposed	0 / 50 (0.00%)	4 / 52 (7.69%)	1 / 35 (2.86%)
occurrences (all)	0	12	2
Lymphocyte count decreased			

subjects affected / exposed	3 / 50 (6.00%)	2 / 52 (3.85%)	1 / 35 (2.86%)
occurrences (all)	38	4	2
Neutrophil count decreased			
subjects affected / exposed	12 / 50 (24.00%)	11 / 52 (21.15%)	3 / 35 (8.57%)
occurrences (all)	114	100	32
Platelet count decreased			
subjects affected / exposed	3 / 50 (6.00%)	4 / 52 (7.69%)	2 / 35 (5.71%)
occurrences (all)	28	12	6
Weight decreased			
subjects affected / exposed	6 / 50 (12.00%)	25 / 52 (48.08%)	14 / 35 (40.00%)
occurrences (all)	12	60	28
White blood cell count decreased			
subjects affected / exposed	9 / 50 (18.00%)	12 / 52 (23.08%)	3 / 35 (8.57%)
occurrences (all)	102	108	16
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	6	0	4
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	3 / 50 (6.00%)	0 / 52 (0.00%)	1 / 35 (2.86%)
occurrences (all)	6	0	2
Headache			
subjects affected / exposed	5 / 50 (10.00%)	5 / 52 (9.62%)	5 / 35 (14.29%)
occurrences (all)	10	12	10
Dysgeusia			
subjects affected / exposed	1 / 50 (2.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	2	4	4
Dizziness			
subjects affected / exposed	4 / 50 (8.00%)	4 / 52 (7.69%)	4 / 35 (11.43%)
occurrences (all)	10	8	12
Lethargy			
subjects affected / exposed	2 / 50 (4.00%)	3 / 52 (5.77%)	1 / 35 (2.86%)
occurrences (all)	4	6	2
Neuropathy peripheral			

subjects affected / exposed	6 / 50 (12.00%)	5 / 52 (9.62%)	3 / 35 (8.57%)
occurrences (all)	16	10	8
Taste disorder			
subjects affected / exposed	0 / 50 (0.00%)	3 / 52 (5.77%)	2 / 35 (5.71%)
occurrences (all)	0	6	4
Polyneuropathy			
subjects affected / exposed	4 / 50 (8.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences (all)	8	2	2
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 50 (6.00%)	3 / 52 (5.77%)	3 / 35 (8.57%)
occurrences (all)	6	6	6
Tremor			
subjects affected / exposed	2 / 50 (4.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	4	0	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	23 / 50 (46.00%)	26 / 52 (50.00%)	11 / 35 (31.43%)
occurrences (all)	110	98	38
Lymphopenia			
subjects affected / exposed	3 / 50 (6.00%)	1 / 52 (1.92%)	3 / 35 (8.57%)
occurrences (all)	22	2	8
Leukopenia			
subjects affected / exposed	7 / 50 (14.00%)	11 / 52 (21.15%)	4 / 35 (11.43%)
occurrences (all)	56	38	12
Leukocytosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	4
Neutropenia			
subjects affected / exposed	14 / 50 (28.00%)	11 / 52 (21.15%)	8 / 35 (22.86%)
occurrences (all)	100	46	42
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 50 (2.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	2	6	8
Abdominal pain			

subjects affected / exposed	2 / 50 (4.00%)	3 / 52 (5.77%)	0 / 35 (0.00%)
occurrences (all)	4	6	0
Constipation			
subjects affected / exposed	6 / 50 (12.00%)	7 / 52 (13.46%)	7 / 35 (20.00%)
occurrences (all)	14	14	14
Diarrhoea			
subjects affected / exposed	12 / 50 (24.00%)	33 / 52 (63.46%)	21 / 35 (60.00%)
occurrences (all)	36	170	80
Haemorrhoids			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	2 / 35 (5.71%)
occurrences (all)	0	2	6
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 50 (2.00%)	1 / 52 (1.92%)	3 / 35 (8.57%)
occurrences (all)	2	2	6
Flatulence			
subjects affected / exposed	0 / 50 (0.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	4
Dyspepsia			
subjects affected / exposed	1 / 50 (2.00%)	3 / 52 (5.77%)	5 / 35 (14.29%)
occurrences (all)	6	6	10
Nausea			
subjects affected / exposed	12 / 50 (24.00%)	21 / 52 (40.38%)	17 / 35 (48.57%)
occurrences (all)	30	56	50
Stomatitis			
subjects affected / exposed	2 / 50 (4.00%)	13 / 52 (25.00%)	7 / 35 (20.00%)
occurrences (all)	6	34	24
Vomiting			
subjects affected / exposed	6 / 50 (12.00%)	14 / 52 (26.92%)	4 / 35 (11.43%)
occurrences (all)	14	36	10
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	16 / 50 (32.00%)	13 / 52 (25.00%)	8 / 35 (22.86%)
occurrences (all)	32	26	16
Dry skin			
subjects affected / exposed	1 / 50 (2.00%)	4 / 52 (7.69%)	2 / 35 (5.71%)
occurrences (all)	2	8	4

Pruritus			
subjects affected / exposed	6 / 50 (12.00%)	6 / 52 (11.54%)	5 / 35 (14.29%)
occurrences (all)	18	14	12
Rash			
subjects affected / exposed	15 / 50 (30.00%)	13 / 52 (25.00%)	5 / 35 (14.29%)
occurrences (all)	50	30	12
Rash maculo-papular			
subjects affected / exposed	0 / 50 (0.00%)	5 / 52 (9.62%)	2 / 35 (5.71%)
occurrences (all)	0	10	4
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 50 (6.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences (all)	6	2	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 50 (18.00%)	4 / 52 (7.69%)	4 / 35 (11.43%)
occurrences (all)	20	10	8
Back pain			
subjects affected / exposed	8 / 50 (16.00%)	7 / 52 (13.46%)	4 / 35 (11.43%)
occurrences (all)	18	16	8
Muscle spasms			
subjects affected / exposed	1 / 50 (2.00%)	4 / 52 (7.69%)	1 / 35 (2.86%)
occurrences (all)	2	8	2
Muscular weakness			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	4
Musculoskeletal chest pain			
subjects affected / exposed	3 / 50 (6.00%)	1 / 52 (1.92%)	2 / 35 (5.71%)
occurrences (all)	6	2	6
Myalgia			
subjects affected / exposed	4 / 50 (8.00%)	2 / 52 (3.85%)	2 / 35 (5.71%)
occurrences (all)	10	4	8
Pain in extremity			
subjects affected / exposed	8 / 50 (16.00%)	3 / 52 (5.77%)	1 / 35 (2.86%)
occurrences (all)	18	6	2
Infections and infestations			

COVID-19			
subjects affected / exposed	11 / 50 (22.00%)	5 / 52 (9.62%)	3 / 35 (8.57%)
occurrences (all)	30	12	6
Paronychia			
subjects affected / exposed	2 / 50 (4.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	6	0	4
Upper respiratory tract infection			
subjects affected / exposed	2 / 50 (4.00%)	5 / 52 (9.62%)	1 / 35 (2.86%)
occurrences (all)	8	10	4
Urinary tract infection			
subjects affected / exposed	4 / 50 (8.00%)	4 / 52 (7.69%)	2 / 35 (5.71%)
occurrences (all)	24	10	8
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 50 (10.00%)	14 / 52 (26.92%)	8 / 35 (22.86%)
occurrences (all)	12	30	18
Diabetes mellitus			
subjects affected / exposed	0 / 50 (0.00%)	1 / 52 (1.92%)	3 / 35 (8.57%)
occurrences (all)	0	2	12
Hyperglycaemia			
subjects affected / exposed	8 / 50 (16.00%)	38 / 52 (73.08%)	19 / 35 (54.29%)
occurrences (all)	32	170	54
Hypertriglyceridaemia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 52 (0.00%)	2 / 35 (5.71%)
occurrences (all)	2	0	4
Hypocalcaemia			
subjects affected / exposed	2 / 50 (4.00%)	3 / 52 (5.77%)	3 / 35 (8.57%)
occurrences (all)	14	10	6
Hypoalbuminaemia			
subjects affected / exposed	2 / 50 (4.00%)	2 / 52 (3.85%)	3 / 35 (8.57%)
occurrences (all)	12	4	6
Hyperuricaemia			
subjects affected / exposed	3 / 50 (6.00%)	1 / 52 (1.92%)	1 / 35 (2.86%)
occurrences (all)	14	4	4
Hypokalaemia			

subjects affected / exposed	3 / 50 (6.00%)	13 / 52 (25.00%)	5 / 35 (14.29%)
occurrences (all)	10	44	16
Hyponatraemia			
subjects affected / exposed	2 / 50 (4.00%)	3 / 52 (5.77%)	3 / 35 (8.57%)
occurrences (all)	8	8	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2021	The main purposes of this amendment were to: ● incorporate guidance related to the use of SGLT2 inhibitors for the management of hyperglycemia, an on-target side effect of the PI3K inhibitor alpelisib, ● incorporate further guidance on alpelisib associated rash and its optimal management. ● implement a separate biomarker prescreening ICF to allow greater flexibility to investigators and sites in pre identifying potential study participants that meet the required biomarker profile. ● allow TNBC patients with tumor harboring PTEN loss and unknown PIK3CA status to enroll into study Part B1. In addition, language related to a Public Health emergency was added, wording was aligned to Novartis protocol template v4.0 language and clarifications and updates in response to health authority feedback were incorporated.
14 March 2023	The main purpose of this amendment was to modify the study conduct and data analysis following the recruitment halt on 11-Nov-2022 in Part A due to slow recruitment. Part B1 did not meet its primary objective for confirmed ORR. Therefore, Part B2 was not initiated, recruitment was halted for the entire study and the primary analysis for Part A was descriptive only. Ongoing participants were allowed to continue study treatment if they derived benefits as assessed by the investigator. Significant changes included: ● Adjustment of objectives and endpoints due to limited sample size in Part A (descriptive primary analysis, OS would be a secondary rather than a key secondary endpoint, PK, PROs, and time to deterioration of ECOG performance status were moved from secondary to exploratory endpoints). ● Allowed unblinding of all participants in Part A for investigators to know participant's current treatment allocation. ● Safety and efficacy assessments once all participants had completed 6 months of study treatment or had discontinued from study treatment were streamlined. ● The protocol was updated based on the Investigator's Brochure Edition 17.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported