Clinical trial results:
Open-label, multicenter, pilot-trial evaluating the safety and utility of a hybrid decentralized clinical trial (DCT) approach using a TELEmedicine platform in patients with HR-positive/HER2-negative advanced breast cancer with a PIK3CA mutation treated with alpelisib – fulvestrant TELEPIK Trial

Summary

EudraCT number	2020-005882-15
Trial protocol	SE
Global end of trial date	19 September 2022

Results information

Result version number	v1 (current)
This version publication date	07 July 2023
First version publication date	07 July 2023

Trial information

Trial identification

Sponsor protocol code	CBYL719A03201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04862143
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
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	19 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess participant satisfaction with the decentralized clinical trial (DCT) experience.

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 March 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 1 center from Sweden

Pre-assignment

Screening details:

The screening phase began once written informed consent was provided and ended after 28 days or when subject was enrolled, whichever came first.

Period 1

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

Arms

Arm title	Alpelisib + fulvestrant

Arm description:

Participants were administered alpelisib at a daily dose of 300 mg for 12 cycles of 28 days and fulvestrant at a dose of 500 mg via intramuscular injection on Cycle 1 Day 1 and Cycle 1 Day 15, and Day 1 of each subsequent cycle up to Cycle 12. Pre-menopausal women also received goserelin at a dose of 3.6 mg on Day 1 of each cycle.

Arm type	Experimental
Investigational medicinal product name	Alpelisib
Investigational medicinal product code	BYL719
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received a daily oral dose of 300 mg of alpelisib film-coated tablets for a total of 12 cycles, with each cycle lasting 28 days.

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered fulvestrant at a dose of 500 mg via intramuscular injection on Cycle 1 Day 1 and Cycle 1 Day 15, and on Day 1 of each 28-day cycle thereafter until Cycle 12.

Investigational medicinal product name	Goserelin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pre-menopausal women were administered a dose of 3.6 mg of goserelin injection via intramuscular route, beginning on Cycle 1 Day 1. Subsequently, the same dose was administered on Day 1 of each 28-day cycle throughout the study.

Number of subjects in period 1	Alpelisib + fulvestrant
Started	2
Completed	0
Not completed	2
Adverse event, non-fatal	1
Study terminated by sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	Alpelisib + fulvestrant
Reporting group description:	
Participants were administered alpelisib at a daily dose of 300 mg for 12 cycles of 28 days and fulvestrant at a dose of 500 mg via intramuscular injection on Cycle 1 Day 1 and Cycle 1 Day 15, and Day 1 of each subsequent cycle up to Cycle 12. Pre-menopausal women also received goserelin at a dose of 3.6 mg on Day 1 of each cycle.	

Reporting group values	Alpelisib + fulvestrant	Total	
Number of subjects	2	2	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	2	2	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	54		
standard deviation	± 0	-	
Sex/Gender, Customized			
Gender details were not collected from any participant			
Units: Participants			
Unknown	2	2	

End points

End points reporting groups

Reporting group title	Alpelisib + fulvestrant

Reporting group description:

Participants were administered alpelisib at a daily dose of 300 mg for 12 cycles of 28 days and fulvestrant at a dose of 500 mg via intramuscular injection on Cycle 1 Day 1 and Cycle 1 Day 15, and Day 1 of each subsequent cycle up to Cycle 12. Pre-menopausal women also received goserelin at a dose of 3.6 mg on Day 1 of each cycle.

Primary: Participant satisfaction assessed through the trial feedback questionnaire (TFQ)

End point title	Participant satisfaction assessed through the trial feedback questionnaire (TFQ)[1]

End point description:

The TFQ was designed to capture the patient's experience during a clinical trial. The questionnaire consisted of 23 questions that assessed various aspects of the trial experience. Each question in the TFQ scored on a scale ranging from 1 (representing the worst response) to 5 (representing the best response). To calculate the total score, the scores obtained from each of the 23 questions were summed up. The resulting sum represented the participant's total score, which could ranged from 23 (indicating the lowest possible score) to 115 (indicating the highest possible score).
"9999" values indicate that there was not sufficient data available to calculate the value.

End point type	Primary

End point timeframe:

Baseline, and on Day 1 of Cycle 4 and 7. Cycle= 28 days

Notes:

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

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Score on a Scale				
median (full range (min-max))				
Baseline (n=2)	99.5 (92 to 107)			
Cycle 4 Day 1 (n=1)	89 (-9999 to 9999)			
Cycle 7 Day 1 (n=1)	98 (-9999 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Patient retention on the decentralized clinical trial (DCT) approach

End point title	Patient retention on the decentralized clinical trial (DCT) approach

End point description:

Patient retention on the DCT approach was calculated as the percentage of participants on remote monitoring for participants still on treatment

End point type	Secondary

End point timeframe:

At 3 and 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants				
3 months	1			
6 months	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of unscheduled in-clinic visits because of safety reasons

End point title	Number of unscheduled in-clinic visits because of safety reasons

End point description:

Unscheduled in-clinic visits were defined as visits that were originally intended to be conducted remotely but were ultimately carried out on-site, or visits that were not originally scheduled but took place on-site or at the local oncologist's (regional hospital).
The total number of unscheduled in-clinic visits that were prompted by safety reasons was evaluated

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of study, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Visits	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose reductions/interruptions for alpelisib

End point title	Number of participants with dose reductions/interruptions for

	alpelisib

End point description:

Number of participants with dose reductions and interruptions for alpelisib

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of treatment, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants				
Dose interruptions	1			
Dose reductions	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinue treatment due to adverse events (AEs)

End point title	Number of participants who discontinue treatment due to adverse events (AEs)

End point description:

An AE refers to any untoward medical occurrence, such as an unfavorable and unintended sign (including abnormal laboratory findings), symptom, or disease.
The number of participants who discontinued the treatment due to adverse events was evaluated

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of treatment, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of unscheduled in-clinic visits per participant in the study

End point title	Number of unscheduled in-clinic visits per participant in the

	study

End point description:

Unscheduled in-clinic visits were defined as visits that were originally intended to be conducted remotely but were ultimately carried out on-site, or visits that were not originally scheduled but took place on-site or at the local oncologist's (regional hospital).
The total number of unscheduled in-clinic visits per participants was evaluated

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of study, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Visits per participant	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of unscheduled in-clinic visits

End point title	Number of unscheduled in-clinic visits

End point description:

Unscheduled in-clinic visits were defined as visits that were originally intended to be conducted remotely but were ultimately carried out on-site, or visits that were not originally scheduled but took place on-site or at the local oncologist's (regional hospital).
The total number of unscheduled in-clinic visits was evaluated

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of study, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Visits	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Adverse events of special interest (AESIs)-hyperglicemia, rash and diarrhea

End point title	Number of participants with Adverse events of special interest (AESIs)- hyperglicemia, rash and diarrhea

End point description:

AESIs (Adverse Events of Special Interest) are defined as events, whether serious or non-serious, that are of scientific and medical concern specific to the sponsor's product or program. These events may require ongoing monitoring and communication by the investigator to the sponsor. For this study, the following AESIs were defined: hyperglycemia, rash, and diarrhea.
The number of participants experiencing these events per the Common Terminology Criteria for Adverse Events (CTCAE) v4.03 was evaluated.

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of study, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants				
Diarrhea	1			
Hyperglycaemia	2			
Rash	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Adverse Events (AEs) leading to in-clinic visits

End point title	Number of participants with Adverse Events (AEs) leading to in-clinic visits

End point description:

An AE refers to any untoward medical occurrence, such as an unfavorable and unintended sign (including abnormal laboratory findings), symptom, or disease.
The number of participants with AEs per the Common Terminology Criteria for Adverse Events (CTCAE) v4.03 leading to in-clinic visits was assessed.

End point type	Secondary

End point timeframe:

From the date of the first study treatment up to the end of study, assessed up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)

End point title	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)

End point description:

The EORTC QLQ-C30 questionnaire contained 30 items and was composed of both multi-item scales and single item measures. These included five functional scales (physical, role, emotional, cognitive, and social functioning), three symptom scales (fatigue, nausea/vomiting, and pain), six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial impact), and a global health status/quality of life (QoL) scale.
All of the scales and single items ranged from 0 to 100. A high scale score represented a higher response level. Thus, a high score for a functional scale indicated a high/healthy level of functioning, a high score for the QoL indicated high QoL, but a high score for a symptom scale/single item indicated a high level of symptomatology/problems.
The EORTC QLQ-C30 scores for all functional and symptom scales were evaluated.
"9999" values indicate that there was not sufficient data available to calculate the value.

End point type	Secondary

End point timeframe:

Baseline, and on Day 1 of Cycle 4, and 7 and end of treatment, assessed up to 6 months. Cycle= 28 days

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Score on a Scale				
median (full range (min-max))				
QoL- Baseline (n=2)	75 (67 to 83)			
QoL- Cycle 4 Day 1 (n=1)	83 (-9999 to 9999)			
QoL- Cycle 7 Day 1 (n=1)	92 (-9999 to 9999)			
QoL- End of Treatment (n=2)	75 (67 to 83)			
Physical Functioning- Baseline (n=2)	90 (80 to 100)			
Physical Functioning- Cycle 4 Day 1 (n=1)	93 (-9999 to 9999)			
Physical Functioning- Cycle 7 Day 1 (n=1)	100 (-9999 to 9999)			
Physical Functioning-End of Treatment (n=2)	86.5 (80 to 93)			
Role Functioning- Baseline (n=2)	91.5 (83 to 100)			
Role Functioning- Cycle 4 Day 1 (n=1)	100 (-9999 to 9999)			
Role Functioning- Cycle 7 Day 1 (n=1)	100 (-9999 to 9999)			
Role Functioning-End of Treatment (n=2)	83.5 (67 to 100)			
Emotional Functioning- Baseline (n=2)	71 (67 to 75)			
Emotional Functioning- Cycle 4 Day 1 (n=1)	83 (-9999 to 9999)			

Emotional Functioning- Cycle 7 Day 1 (n=1)	92 (-9999 to 9999)			
Emotional Functioning- End of treatment (n=2)	83 (83 to 83)			
Cognitive Functioning- Baseline (n=2)	91.5 (83 to 100)			
Cognitive Functioning- Cycle 4 Day 1 (n=1)	100 (-9999 to 9999)			
Cognitive Functioning- Cycle 7 Day 1 (n=1)	100 (-9999 to 9999)			
Cognitive Functioning- End of treatment (n=2)	75 (67 to 83)			
Social Functioning- Baseline (n=2)	91.5 (83 to 100)			
Social Functioning- Cycle 4 Day 1 (n=1)	100 (-9999 to 9999)			
Social Functioning- Cycle 7 Day 1 (n=1)	100 (-9999 to 9999)			
Social Functioning- End of treatment (n=2)	91.5 (83 to 100)			
Fatigue- Baseline (n=2)	22 (0 to 44)			
Fatigue- Cycle 4 Day 1 (n=1)	22 (-9999 to 9999)			
Fatigue- Cycle 7 Day 1 (n=1)	0 (-9999 to 9999)			
Fatigue- End of treatment (n=2)	33 (22 to 44)			
Nausea/vomiting- Baseline (n=2)	0 (0 to 0)			
Nausea/vomiting- Cycle 4 Day 1 (n=1)	17 (-9999 to 9999)			
Nausea/vomiting- Cycle 7 Day 1 (n=1)	0 (-9999 to 9999)			
Nausea/vomiting- End of treatment (n=2)	0 (0 to 0)			
Pain- Baseline (n=2)	8.5 (0 to 17)			
Pain- Cycle 4 Day 1 (n=1)	0 (-9999 to 9999)			
Pain- Cycle 7 Day 1 (n=1)	0 (-9999 to 9999)			
Pain- End of treatment (n=2)	16.5 (0 to 33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Brief Pain Inventory Short Form (BPI-SF) scores

End point title	Brief Pain Inventory Short Form (BPI-SF) scores

End point description:

The BPI-SF was a questionnaire used to assess pain intensity and interference with daily activities. The Pain Severity Subscale included four questions asking individuals to rate their pain intensity on a scale from 0 to 10, with higher scores indicating more severe pain. The Pain Interference Subscale consisted of seven items that assessed how pain had interfered with activities, rated on the same scale. Both subscales had a total score range of 0 to 10, with higher scores indicating more significant pain or interference.

End point type	Secondary

End point timeframe:

Baseline, and on Day 1 of Cycle 4, and 7 and end of treatment, assessed up to 6 months. Cycle= 28

days

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Score on a scale				
median (full range (min-max))				
Pain severity- Baseline (n=2)	1.63 (1.25 to 2.00)			
Pain severity- Cycle 4 Day 1 (n=1)	0 (-9999 to 9999)			
Pain severity- Cycle 7 Day 1 (n=1)	0.75 (-9999 to 9999)			
Pain severity- End of treatment (n=2)	1.13 (0.00 to 2.25)			
Pain interference- Baseline (n=2)	0.79 (0.00 to 1.57)			
Pain interference- Cycle 4 Day 1 (n=1)	0 (-9999 to 9999)			
Pain interference- Cycle 7 Day 1 (n=1)	0 (-9999 to 9999)			
Pain interference- End of treatment (n=2)	1.07 (0 to 2.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQol 5-Dimension 5-Level (EQ-5D-5L)- Visual analog scale (VAS) score

End point title	EuroQol 5-Dimension 5-Level (EQ-5D-5L)- Visual analog scale (VAS) score

End point description:

The 5-level EQ-5D (EQ-5D-5L) questionnaire is a standardized measure of health status. The EQ-5D descriptive system comprises of the 5 following dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Along with the five dimensions of health, the EQ-5D-5L includes a VAS where respondents rate their overall health status on a scale from 0 to 100, where 0 represents the worst possible health state and 100 represents the best possible health state.
The EQ-5D-5L VAS scores were evaluated.
"9999" values indicate that there was not sufficient data available to calculate the value.

End point type	Secondary

End point timeframe:

Baseline, and on Day 1 of Cycle 4, and 7 and end of treatment, assessed up to 6 months. Cycle= 28 days

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Score on a scale				
median (full range (min-max))				
Baseline (n=2)	80 (75 to 85)			
Cycle 4 Day 1 (n=1)	93 (-9999 to 9999)			
Cycle 7 Day 1 (n=1)	95 (-9999 to 9999)			
End of treatment (n=2)	82.5 (70 to 95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with progression-free survival (PFS) according to RECIST 1.1

End point title	Number of participants with progression-free survival (PFS) according to RECIST 1.1

End point description:

The number of participants with PFS was defined as the count of participants who did not experience disease progression or death due to any cause during the study. Progression was assessed by the Response Evaluation Criteria in Solid Tumors (RECIST)v1.1 based on local radiology review

End point type	Secondary

End point timeframe:

Up to 6 months

End point values	Alpelisib + fulvestrant			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Participants	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start up to end of study, assessed up to 6 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	Alpelisib + fulvestrant

Reporting group description:

Participants were administered alpelisib at a daily dose of 300 mg for 12 cycles of 28 days and fulvestrant at a dose of 500 mg via intramuscular injection on Cycle 1 Day 1 and Cycle 1 Day 15, and Day 1 of each subsequent cycle up to Cycle 12. Pre-menopausal women also received goserelin at a dose of 3.6 mg on Day 1 of each cycle.

Serious adverse events	Alpelisib + fulvestrant		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Alpelisib + fulvestrant		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)		
Investigations			
Weight decreased			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 2 (100.00%)		
occurrences (all)	2		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all)	2 / 2 (100.00%) 2		
Abdominal pain subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Diarrhea subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Dry mouth subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Gastritis subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Stomatitis subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 2 (100.00%) 18		
Decreased appetite subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2021	The protocol was amended to address the request for supplementary information as described in the Deficiency letter received from the Swedish Health Authority (Medical Products Agency) on 22 April 2021 before the study started. The amended version was in accordance with the responses indicated by Novartis on 29 April 2021.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com for complete trial results.

Notes: