Clinical trial results:
A RANDOMIZED, OPEN-LABEL, MULTI-CENTER PHASE IV STUDY EVALUATING PALBOCICLIB PLUS ENDOCRINE TREATMENT VERSUS A CHEMOTHERAPY-BASED TREATMENT STRATEGY IN PATIENTS WITH HORMONE RECEPTOR POSITIVE / HER2 NEGATIVE METASTATIC BREAST CANCER IN A REAL WORLD SETTING.

Summary

EudraCT number	2016-004482-89
Trial protocol	DE
Global end of trial date	30 August 2024

Results information

Result version number	v1 (current)
This version publication date	15 August 2025
First version publication date	15 August 2025

Trial information

Trial identification

Sponsor protocol code	GBG93

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	BfArM number: 4042230, ClinicalTrials.gov: NCT03355157

Notes:

Sponsors

Sponsor organisation name	GBG Forschungs GmbH
Sponsor organisation address	Dornhofstr. 10, Neu-Isenburg, Germany, 63263
Public contact	Medicine and Research, GBG Forschungs GmbH, +49 610274800, publications@gbg.de
Scientific contact	Medicine and Research, GBG Forschungs GmbH, +49 610274800, publications@gbg.de

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	06 June 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2024
Global end of trial reached?	Yes
Global end of trial date	30 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the time-to-treatment failure (TTF) for patients randomized to receive pre-defined chemotherapy treatment strategy versus those randomized to receive palbociclib and endocrine therapy.

Protection of trial subjects:

The trial protocol including amendments, the patient information and the informed consent were reviewed and approved from a properly constituted IRB/IEC for each site prior to the study start.
The trial was in compliance with the International Conference on Harmonization (ICH) - Harmonized Tripartite Guideline for Good Clinical Practice (GCP) (E6), and the Commission Directives in the European Community as well as with the applicable German national laws and regulations, and with Declaration of Helsinki and its revisions in all aspects of preparation, monitoring, reporting, auditing, and archiving.

Background therapy:

in palbociclib arm:
endocrine treatment by Aromatase inhibitors (exemestane or letrozole) or fulvestrant as per label in the respective country

in comparator arm:
physicians choice mono-chemotherapy (capecitabine, epirubicin, paclitaxel or vinorelbine i.v.; having either an approved label in the respective countries and/or is supported by guidelines for the treatment of first-line MBC) with or without an endocrine maintenance therapy after chemotherapy with Tamoxifen, aromatase inhibitors (exemestane or letrozole) or fulvestrant as per label in the respective country.

Evidence for comparator:

no comparator drug

Actual start date of recruitment	30 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 130
Worldwide total number of subjects	130
EEA total number of subjects	130

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)	75
From 65 to 84 years	53
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Study run only in Germany, 28 sites recruited 130 patients.
Start of recruitment = April 2018
First Pat in = 17-Apr-2018
Last Pat in = 15-Dec-2023
Last Pat completed = 1-Aug-2024
65 Pat randomized to each study arm
10 Pat revoke consent prior to treatment
61 Pat in arm: palbociclib + estrogen therapy
59 Pat in arm: chemotherapy

Pre-assignment

Screening details:

Fe/male pat's with histol. confirmed symptomatic/asymptomatic metastatic invasive HR+ and HER2 neg breast cancer, excluding asymptom. oligometastases of bone as the only site of metastatic disease; pat's have a life-expectancy >6 months and in opinion of treating physician are candidates suitable for randomization for mono-chem. therapy treatment.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Palbociclib + endocrine therapy

Arm description:

Palbociclib 125mg, hard capsules + Endocrine Therapy (ET)
ET: aromatase inhibitors exemestane or letrozole or fulvestrant as per label in the respective countries.

Letrozole 2.5 mg orally once a day
Exemestane 25 mg orally once a day
Fulvestrant 2x 250 mg injections i.m. on Day 1 and Day 15 in the first month followed by 2x 250 mg on Day 1 every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Palbociclib 125mg, hard capsules
Investigational medicinal product code	100000163078
Other name	Ibrance
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Palbociclib hard capsules, at a dose of 125 mg, orally, once a day, at the same day time, with food for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days.

Arm title	Chemotherapy +/- endocrine maintenance therapy

Arm description:

Physician´s choice mono-chemotherapy (capecitabine, epirubicin, paclitaxel or vinorelbine i.v.) having either an approved label in the respective countries and/or is supported by guidelines for the treatment of first-line metastatic breast cancer.

Endocrine therapy as maintenance therapy after chemotherapy: Tamoxifen, aromatase inhibitors (exemestane or letrozole) or fulvestrant as per label in the respective countries.

Arm type	Physician´s choice mono-chemotherap

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy
Started	65	65
Completed	15	4
Not completed	50	61
Initiation of altern/prohibited anti-cancer therap	-	2
Death	5	2
never started treatment	4	6
Second primary of non-breast cancers	1	-
Adverse event	3	2
Patient's decision	5	5
patient got lost	-	1
Progressive disease	32	42
Use of radiotherapy not indicated at baseline	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Palbociclib + endocrine therapy
Reporting group description:	
Palbociclib 125mg, hard capsules + Endocrine Therapy (ET) ET: aromatase inhibitors exemestane or letrozole or fulvestrant as per label in the respective countries. Letrozole 2.5 mg orally once a day Exemestane 25 mg orally once a day Fulvestrant 2x 250 mg injections i.m. on Day 1 and Day 15 in the first month followed by 2x 250 mg on Day 1 every 4 weeks	
Reporting group title	Chemotherapy +/- endocrine maintenance therapy
Reporting group description:	
Physician´s choice mono-chemotherapy (capecitabine, epirubicin, paclitaxel or vinorelbine i.v.) having either an approved label in the respective countries and/or is supported by guidelines for the treatment of first-line metastatic breast cancer. Endocrine therapy as maintenance therapy after chemotherapy: Tamoxifen, aromatase inhibitors (exemestane or letrozole) or fulvestrant as per label in the respective countries.	

Reporting group values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy	Total
Number of subjects	65	65	130
Age categorical			
Units: Subjects			

Age continuous			
age at randomization			
Units: years			
median	63	62	
full range (min-max)	42 to 85	31 to 80	-
Gender categorical			
gender at randomization			
Units: Subjects			
Female	64	63	127
Male	1	2	3

End points

End points reporting groups

Reporting group title	Palbociclib + endocrine therapy

Reporting group description:

Palbociclib 125mg, hard capsules + Endocrine Therapy (ET)
ET: aromatase inhibitors exemestane or letrozole or fulvestrant as per label in the respective countries.

Letrozole 2.5 mg orally once a day
Exemestane 25 mg orally once a day
Fulvestrant 2x 250 mg injections i.m. on Day 1 and Day 15 in the first month followed by 2x 250 mg on Day 1 every 4 weeks

Reporting group title	Chemotherapy +/- endocrine maintenance therapy

Reporting group description:

Physician´s choice mono-chemotherapy (capecitabine, epirubicin, paclitaxel or vinorelbine i.v.) having either an approved label in the respective countries and/or is supported by guidelines for the treatment of first-line metastatic breast cancer.

Endocrine therapy as maintenance therapy after chemotherapy: Tamoxifen, aromatase inhibitors (exemestane or letrozole) or fulvestrant as per label in the respective countries.

Primary: Time to treatment failure (TTF), mITT analysis set

End point title	Time to treatment failure (TTF), mITT analysis set

End point description:

Treatment failure rate (TF) at 6 months.

Intercurrent events:
- change of endocrine maintenance therapy (change within the class of aromatase inhibitors was not considered as a TF)
- prohibited anticancer medication was used
- use of radiotherapy
- pat switched from palbo+ET to CT arm or vice versa
- pat was lost during study treatment
- change from one mono-CT agent to another or the use of poly-chemotherapy (change of CT before start of treatment, or extension of CT treatment compared to the initial treatment plan was not considered as TF)

Also, the discontinuation due to investigator’s decision was not considered as TF.

End point type	Primary

End point timeframe:

TTF was defined as time from randomization to treatment failure due to disease progression, treatment toxicity, patient’s preference, or death or intercurrent event (refer to description).

End point values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: percent				
number (confidence interval 80%)	66.7 (58.2 to 73.8)	50.8 (42.2 to 58.8)		

Statistical analyses

Statistical analysis title	Hazard ratio
Statistical analysis description:	
Additionally, the 95% CI for the hazard ratio was provided: hazard ratio = 0.46 (95% CI, 0.31, 0.69).	
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.46
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.35
upper limit	0.6

Statistical analysis title	Two-sided log-rank test
Statistical analysis description:	
The difference in TTF was tested using a two-sided log-rank test with significance level of alpha = 0.2 .	
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Logrank

Secondary: Time to first subsequent treatment (TFST), mITT analysis set

End point title	Time to first subsequent treatment (TFST), mITT analysis set
End point description:	
Time to first subsequent treatment (TFST) was defined as the time from randomization to start of first subsequent anticancer treatment or death. Note: anticancer treatment actually comprised all sorts of treatment such as ET, chemotherapy, targeted therapy etc.	
End point type	Secondary
End point timeframe:	
Time from randomization to first subsequent anticancer treatment (including chemotherapy, endocrine or targeted therapy) after EOT, or death.	

End point values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: percent				
number (confidence interval 80%)	78.2 (70.3 to 84.2)	68.4 (59.8 to 75.6)		

Statistical analyses

Statistical analysis title	Hazard ratio
Statistical analysis description:	
Additionally, the 95% CI for the hazard ratio was provided: hazard ratio = 0.50 (95% CI, 0.32, 0.77).	
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.37
upper limit	0.66

Statistical analysis title	Two-sided log-rank test
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0015
Method	Logrank

Secondary: Time to first subsequent chemotherapy (TFSCT), mITT analysis set

End point title	Time to first subsequent chemotherapy (TFSCT), mITT analysis set

End point description:

Restricted mean survival time (RMST) for TFSCT in months.
The proportional hazard assumption is violated for TFSCT; therefore, the hazard ratio may not be an

adequate measure of effect, and the log-rank test was not an appropriate test here. Instead, the restricted mean survival time (RMST) until tau=38 months with the corresponding adequate test (Wald-type test using an approximate Chi-square statistic) for comparison of the RMST between treatment arms was performed. Tau was chosen according to the smaller maximum observation time of an event in both arms. The RMST, the area under the survival curve between 0 and tau=38 months, is the estimate of the mean survival time in this time interval.

End point type	Secondary

End point timeframe:

Time from randomization to start of first subsequent anticancer chemotherapy or death (TFSCT).

End point values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: percent				
number (confidence interval 95%)	23.9 (20.1 to 27.6)	25.0 (21.3 to 28.6)		

Statistical analyses

Statistical analysis title	Test for comparison of RMST

Statistical analysis description:

The restricted mean survival time (RMST) until tau=38 months with the corresponding adequate test (Wald-type test using an approximate Chi-square statistic) for comparison of the RMST between treatment arms was performed. Tau was chosen according to the smaller maximum observation time of an event in both arms. The RMST, the area under the survival curve between 0 and tau=38 months, is the estimate of the mean survival time in this time interval.

Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6744
Method	Wald-type test

Secondary: Time to second subsequent treatment regimen (TSST), mITT analysis set

End point title	Time to second subsequent treatment regimen (TSST), mITT analysis set

End point description:

Restricted mean survival time (RMST) for TSST in months.
The proportional hazard assumption is violated for TSST; therefore, the hazard ratio may not be an adequate measure of effect and the log-rank test not an appropriate test here. Instead, the restricted mean survival time (RMST) until tau=35 months with the corresponding adequate test (Wald-type test using an approximate Chi-square statistic) for comparison of the RMST between treatment arms was performed. Tau was chosen according to the smaller maximum observation time of an event in both arms. The RMST, the area under the survival curve between 0 and tau=35 months, is the estimate of the mean survival time in this time interval.

End point type	Secondary

End point timeframe:

Time from randomization to start of second subsequent treatment regimen (TSST) or death.

End point values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: percent				
number (confidence interval 95%)	24.9 (21.7 to 28.1)	21.5 (18.3 to 24.6)		

Statistical analyses

Statistical analysis title	Test for comparison of RMST
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1332
Method	Wald-type test

Secondary: Overall Survival (OS), mITT analysis set

End point title	Overall Survival (OS), mITT analysis set

End point description:

Restricted mean survival time (RMST) for OS in months.
The proportional hazard assumption is violated for OS; therefore, the hazard ratio may not be an adequate measure of effect and the log-rank test not an appropriate test here. Instead, the RMST until tau=46 months with the corresponding adequate test (Wald-type test using an approximate Chi-square statistic) for comparison of the RMST between treatment arms was performed. Tau was chosen according to the smaller maximum observation time of an event in both arms. The RMST, the area under the survival curve between 0 and tau=46 months, is the estimate of the mean survival time in this time interval.

End point type	Secondary

End point timeframe:

OS is defined as the time from randomization to death due to any reason.

End point values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: percent				
number (confidence interval 95%)	33.6 (29.3 to 37.9)	31.5 (27.1 to 35.9)		

Statistical analyses

Statistical analysis title	Test for comparison of RMST
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4939
Method	Wald-type test

Secondary: Progression free survival (PFS), mITT analysis set

End point title	Progression free survival (PFS), mITT analysis set

End point description:

End point type	Secondary

End point timeframe:

Progression free survival (PFS) is the time from randomization to first progression as assessed by the investigator or death, whichever occurs first.

End point values	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	59		
Units: percent				
number (confidence interval 80%)	71.5 (63.2 to 78.2)	63.0 (54.2 to 70.6)		

Statistical analyses

Statistical analysis title	Hazard ratio

Statistical analysis description:

Additionally, the 95% CI for the hazard ratio was provided: hazard ratio = 0.45 (95% CI, 0.29, 0.70).

Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.34
upper limit	0.6

Statistical analysis title	Two-sided log-rank test
Comparison groups	Palbociclib + endocrine therapy v Chemotherapy +/- endocrine maintenance therapy
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring during the study treatment until 30 days after the last study treatment were reported.
AEs were analyzed according to MedDRA V24 as any grade (1-4) and high-grade (3-4).

Adverse event reporting additional description:

Safety analysis was performed based on the safety analysis set, which consists of 62 patients who were treated with Palbociclib and 58 patients who were treated with chemotherapy.
One patient was randomized in CT arm but was treated with palbociclib from the beginning.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Palbociclib + endocrine therapy

Reporting group description:

The occurrence of AE categories was displayed as
• number and percentage of grades 1-4 (any grade) per treatment group and overall,
• number and percentage of grades 3-4 (high grade) per treatment group and overall,
• number and percentage of patients per grade (none, grade 1, grade 2, grade 3, grade 4) per treatment group and overall.

Reporting group title	Chemotherapy +/- endocrine maintenance therapy

Reporting group description:

The occurrence of AE categories was displayed as
• number and percentage of grades 1-4 (any grade) per treatment group and overall,
• number and percentage of grades 3-4 (high grade) per treatment group and overall,
• number and percentage of patients per grade (none, grade 1, grade 2, grade 3, grade 4) per treatment group and overall.

Serious adverse events	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 62 (29.03%)	16 / 58 (27.59%)	
number of deaths (all causes)	25	24	
number of deaths resulting from adverse events	6	0	
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
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	3 / 62 (4.84%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Lymphadenectomy			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			

subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	3 / 62 (4.84%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	2 / 62 (3.23%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 62 (3.23%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 62 (1.61%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nausea			
subjects affected / exposed	2 / 62 (3.23%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vomiting			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 62 (4.84%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected seroma			

subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 62 (3.23%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Palbociclib + endocrine therapy	Chemotherapy +/- endocrine maintenance therapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 62 (98.39%)	58 / 58 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Other SOC 02			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Embolism			
subjects affected / exposed	4 / 62 (6.45%)	4 / 58 (6.90%)	
occurrences (all)	4	4	
Hot flush			
subjects affected / exposed	18 / 62 (29.03%)	6 / 58 (10.34%)	
occurrences (all)	18	6	
Hypertension			
subjects affected / exposed	3 / 62 (4.84%)	3 / 58 (5.17%)	
occurrences (all)	3	3	
Other SOC 12			
subjects affected / exposed	2 / 62 (3.23%)	2 / 58 (3.45%)	
occurrences (all)	2	2	
Surgical and medical procedures			
Other SOC 25			
subjects affected / exposed	5 / 62 (8.06%)	1 / 58 (1.72%)	
occurrences (all)	5	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	41 / 62 (66.13%)	42 / 58 (72.41%)	
occurrences (all)	41	42	
Oedema peripheral			
subjects affected / exposed	9 / 62 (14.52%)	12 / 58 (20.69%)	
occurrences (all)	9	12	
Pyrexia			
subjects affected / exposed	4 / 62 (6.45%)	2 / 58 (3.45%)	
occurrences (all)	4	2	
Pain			

subjects affected / exposed	4 / 62 (6.45%)	5 / 58 (8.62%)	
occurrences (all)	4	5	
Other SOC 22			
subjects affected / exposed	11 / 62 (17.74%)	6 / 58 (10.34%)	
occurrences (all)	11	6	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 62 (0.00%)	4 / 58 (6.90%)	
occurrences (all)	0	4	
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	2 / 62 (3.23%)	2 / 58 (3.45%)	
occurrences (all)	2	2	
Other SOC 20			
subjects affected / exposed	3 / 62 (4.84%)	2 / 58 (3.45%)	
occurrences (all)	3	2	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	7 / 62 (11.29%)	7 / 58 (12.07%)	
occurrences (all)	7	7	
Dyspnoea			
subjects affected / exposed	19 / 62 (30.65%)	21 / 58 (36.21%)	
occurrences (all)	19	21	
Cough			
subjects affected / exposed	13 / 62 (20.97%)	11 / 58 (18.97%)	
occurrences (all)	13	11	
Pneumonitis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	4 / 62 (6.45%)	6 / 58 (10.34%)	
occurrences (all)	4	6	
Pleuritic pain			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	
occurrences (all)	1	1	
Nasal dryness			

subjects affected / exposed	4 / 62 (6.45%)	2 / 58 (3.45%)	
occurrences (all)	4	2	
Other SOC 13			
subjects affected / exposed	1 / 62 (1.61%)	5 / 58 (8.62%)	
occurrences (all)	1	5	
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 62 (4.84%)	5 / 58 (8.62%)	
occurrences (all)	3	5	
Insomnia			
subjects affected / exposed	6 / 62 (9.68%)	2 / 58 (3.45%)	
occurrences (all)	6	2	
Sleep disorder			
subjects affected / exposed	6 / 62 (9.68%)	6 / 58 (10.34%)	
occurrences (all)	6	6	
Other SOC 07			
subjects affected / exposed	5 / 62 (8.06%)	5 / 58 (8.62%)	
occurrences (all)	5	5	
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	27 / 62 (43.55%)	35 / 58 (60.34%)	
occurrences (all)	27	35	
Alanine aminotransferase increased			
subjects affected / exposed	26 / 62 (41.94%)	27 / 58 (46.55%)	
occurrences (all)	26	27	
Aspartate aminotransferase increased			
subjects affected / exposed	34 / 62 (54.84%)	35 / 58 (60.34%)	
occurrences (all)	34	35	
Blood bilirubin increased			
subjects affected / exposed	7 / 62 (11.29%)	11 / 58 (18.97%)	
occurrences (all)	7	11	
Blood creatinine increased			
subjects affected / exposed	20 / 62 (32.26%)	19 / 58 (32.76%)	
occurrences (all)	20	19	
Blood albumin decreased			

subjects affected / exposed	10 / 62 (16.13%)	9 / 58 (15.52%)	
occurrences (all)	10	9	
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 62 (8.06%)	2 / 58 (3.45%)	
occurrences (all)	5	2	
Other SOC 23			
subjects affected / exposed	8 / 62 (12.90%)	2 / 58 (3.45%)	
occurrences (all)	8	2	
Injury, poisoning and procedural complications			
Other SOC 24			
subjects affected / exposed	10 / 62 (16.13%)	1 / 58 (1.72%)	
occurrences (all)	10	1	
Cardiac disorders			
Other SOC 11			
subjects affected / exposed	2 / 62 (3.23%)	2 / 58 (3.45%)	
occurrences (all)	2	2	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	4 / 62 (6.45%)	10 / 58 (17.24%)	
occurrences (all)	4	10	
Headache			
subjects affected / exposed	10 / 62 (16.13%)	8 / 58 (13.79%)	
occurrences (all)	10	8	
Cognitive disorder			
subjects affected / exposed	6 / 62 (9.68%)	2 / 58 (3.45%)	
occurrences (all)	6	2	
Peripheral sensory neuropathy			
subjects affected / exposed	14 / 62 (22.58%)	21 / 58 (36.21%)	
occurrences (all)	14	21	
Nervous system disorder			
subjects affected / exposed	7 / 62 (11.29%)	9 / 58 (15.52%)	
occurrences (all)	7	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	49 / 62 (79.03%)	35 / 58 (60.34%)	
occurrences (all)	49	35	

Leukopenia			
subjects affected / exposed	59 / 62 (95.16%)	31 / 58 (53.45%)	
occurrences (all)	59	31	
Thrombocytopenia			
subjects affected / exposed	29 / 62 (46.77%)	14 / 58 (24.14%)	
occurrences (all)	29	14	
Neutropenia			
subjects affected / exposed	56 / 62 (90.32%)	14 / 58 (24.14%)	
occurrences (all)	56	14	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	6 / 62 (9.68%)	9 / 58 (15.52%)	
occurrences (all)	6	9	
Other SOC 10			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	
occurrences (all)	1	1	
Dry eye			
subjects affected / exposed	4 / 62 (6.45%)	6 / 58 (10.34%)	
occurrences (all)	4	6	
Other SOC 09			
subjects affected / exposed	4 / 62 (6.45%)	3 / 58 (5.17%)	
occurrences (all)	4	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	22 / 62 (35.48%)	32 / 58 (55.17%)	
occurrences (all)	22	32	
Vomiting			
subjects affected / exposed	9 / 62 (14.52%)	18 / 58 (31.03%)	
occurrences (all)	9	18	
Stomatitis			
subjects affected / exposed	11 / 62 (17.74%)	11 / 58 (18.97%)	
occurrences (all)	11	11	
Dyspepsia			

subjects affected / exposed	6 / 62 (9.68%)	10 / 58 (17.24%)	
occurrences (all)	6	10	
Constipation			
subjects affected / exposed	9 / 62 (14.52%)	10 / 58 (17.24%)	
occurrences (all)	9	10	
Diarrhoea			
subjects affected / exposed	10 / 62 (16.13%)	21 / 58 (36.21%)	
occurrences (all)	10	21	
Gastrointestinal pain			
subjects affected / exposed	4 / 62 (6.45%)	10 / 58 (17.24%)	
occurrences (all)	4	10	
Flatulence			
subjects affected / exposed	2 / 62 (3.23%)	4 / 58 (6.90%)	
occurrences (all)	2	4	
Ascites			
subjects affected / exposed	2 / 62 (3.23%)	0 / 58 (0.00%)	
occurrences (all)	2	0	
Other SOC 14			
subjects affected / exposed	13 / 62 (20.97%)	11 / 58 (18.97%)	
occurrences (all)	13	11	
Hepatobiliary disorders			
Other SOC 15			
subjects affected / exposed	1 / 62 (1.61%)	3 / 58 (5.17%)	
occurrences (all)	1	3	
Skin and subcutaneous tissue disorders			
Skin reaction			
subjects affected / exposed	16 / 62 (25.81%)	17 / 58 (29.31%)	
occurrences (all)	16	17	
Alopecia			
subjects affected / exposed	16 / 62 (25.81%)	16 / 58 (27.59%)	
occurrences (all)	16	16	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 62 (4.84%)	17 / 58 (29.31%)	
occurrences (all)	3	17	
Dry skin			

subjects affected / exposed	3 / 62 (4.84%)	3 / 58 (5.17%)	
occurrences (all)	3	3	
Nail disorder			
subjects affected / exposed	2 / 62 (3.23%)	7 / 58 (12.07%)	
occurrences (all)	2	7	
Other SOC 16			
subjects affected / exposed	10 / 62 (16.13%)	5 / 58 (8.62%)	
occurrences (all)	10	5	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	4 / 62 (6.45%)	2 / 58 (3.45%)	
occurrences (all)	4	2	
Other SOC 18			
subjects affected / exposed	4 / 62 (6.45%)	3 / 58 (5.17%)	
occurrences (all)	4	3	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	21 / 62 (33.87%)	22 / 58 (37.93%)	
occurrences (all)	21	22	
Arthralgia			
subjects affected / exposed	22 / 62 (35.48%)	19 / 58 (32.76%)	
occurrences (all)	22	19	
Myalgia			
subjects affected / exposed	11 / 62 (17.74%)	13 / 58 (22.41%)	
occurrences (all)	11	13	
Back pain			
subjects affected / exposed	5 / 62 (8.06%)	9 / 58 (15.52%)	
occurrences (all)	5	9	
Pain in extremity			
subjects affected / exposed	7 / 62 (11.29%)	6 / 58 (10.34%)	
occurrences (all)	7	6	
Other SOC 17			
subjects affected / exposed	12 / 62 (19.35%)	11 / 58 (18.97%)	
occurrences (all)	12	11	
Infections and infestations			

Infection			
subjects affected / exposed	18 / 62 (29.03%)	16 / 58 (27.59%)	
occurrences (all)	18	16	
COVID-19			
subjects affected / exposed	4 / 62 (6.45%)	3 / 58 (5.17%)	
occurrences (all)	4	3	
Influenza			
subjects affected / exposed	3 / 62 (4.84%)	3 / 58 (5.17%)	
occurrences (all)	3	3	
Nasopharyngitis			
subjects affected / exposed	5 / 62 (8.06%)	6 / 58 (10.34%)	
occurrences (all)	5	6	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	11 / 62 (17.74%)	4 / 58 (6.90%)	
occurrences (all)	11	4	
Hypocalcaemia			
subjects affected / exposed	24 / 62 (38.71%)	24 / 58 (41.38%)	
occurrences (all)	24	24	
Hyperkalaemia			
subjects affected / exposed	27 / 62 (43.55%)	9 / 58 (15.52%)	
occurrences (all)	27	9	
Hypokalaemia			
subjects affected / exposed	9 / 62 (14.52%)	8 / 58 (13.79%)	
occurrences (all)	9	8	
Hypernatraemia			
subjects affected / exposed	6 / 62 (9.68%)	2 / 58 (3.45%)	
occurrences (all)	6	2	
Hyponatraemia			
subjects affected / exposed	18 / 62 (29.03%)	13 / 58 (22.41%)	
occurrences (all)	18	13	
Decreased appetite			
subjects affected / exposed	11 / 62 (17.74%)	11 / 58 (18.97%)	
occurrences (all)	11	11	
Other SOC 06			

subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2	1 / 58 (1.72%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2018	Amendment 1 (Version 9 - 05-JUL-2018): Reduction in the sample size from 360 to 260 patients. Change in the statistical analysis method to a modified intent-to-treat analysis, and deletion of the interim analysis without replacement. The originally planned Actiwatch as an activity tracker for day-night activity was not available to patients and was therefore excluded for operational and organizational reasons, affecting associated secondary objectives and endpoints. Additional whole blood sample (10mL) of each patient were collected before start of study treatment for NGS analysis (optional).
08 August 2020	Amendment 2 (Version 10.1 - 08-AUG-2020): The recruitment period was extended, while the sample size was further reduced from 260 to 150 patients. A report of the genetic tests on the tumor was prepared and made available to the investigator, who could then discuss the results with the patient and provide a copy of the report upon request. Patient information was adapted accordingly, as well as information regarding side effects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported