Clinical trial results:
Phase II open-label, multicenter, randomized trial of neoadjuvant palbociclib in combination with hormonal therapy and HER2 blockade versus paclitaxel in combination with HER2 blockade for postmenopausal patients with hormone receptor positive/HER2 positive early breast cancer

Summary

EudraCT number	2017-005067-40
Trial protocol	BE IT
Global end of trial date	20 April 2023

Results information

Result version number	v1 (current)
This version publication date	28 May 2025
First version publication date	28 May 2025

Trial information

Trial identification

Sponsor protocol code	IBCSG 55-17

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03644186
WHO universal trial number (UTN)	-
Other trial identifiers	Pfizer number: WI223904: Roche number: MO40405

Notes:

Sponsors

Sponsor organisation name	ETOP IBCSG Partners Foundation
Sponsor organisation address	Effingerstrasse 33, Bern, Switzerland, 3008
Public contact	ETOP IBCSG Partners Regulatory Office, ETOP IBCSG Partners Foundation, +41 31 511 94 00, ibcsg-regulatory@etop.ibcsg.org
Scientific contact	ETOP IBCSG Partners Regulatory Office, ETOP IBCSG Partners Foundation, +41 31 511 94 00, ibcsg-regulatory@etop.ibcsg.org

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	20 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2023
Global end of trial reached?	Yes
Global end of trial date	20 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to explore the interaction between the RBsig status and treatment activity, assessed by pathological complete response (pCR), of palbociclib + letrozole versus paclitaxel when given with trastuzumab plus pertuzumab for ER+/HER2+ primary BC.

Protection of trial subjects:

Participating institutions' ethics committees or Institutional Review Boards approved the trial according to local laws and regulations. All patients gave written informed consent, and the trial was performed in compliance with the Helsinki Declaration. The Data Safety and Monitoring Board reviewed the data from this research throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 October 2018
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	Switzerland: 28
Country: Number of subjects enrolled	Belgium: 21
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Italy: 85
Worldwide total number of subjects	147
EEA total number of subjects	119

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)	46
From 65 to 84 years	100
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled on 16 April 2019. The last patient was enrolled on 28 July 2022. The final accrual is 147 patients (target 144).

Pre-assignment

Screening details:

This trial used an IBCSG web-based randomization system, accessed directly by the participating centers. Eligible patients (Appendix A1) were randomized 1:1 to the two treatment arms.

Period 1

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

Blinding implementation details:

none

Arms

Are arms mutually exclusive?	Yes
Arm title	Paclitaxel + HP

Arm description:

Paclitaxel 80 mg/m2 iv on day 1,8,15 every 28 days for 4 cycles
Trastuzumab 600 mg sc every 3 weeks for 5 doses
Pertuzumab 840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m2 iv on day 1,8,15 every 28 days for 4 cycles

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg sc every 3 weeks for 5 doses

Investigational medicinal product name	Pertuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses

Arm title	Palbociclib + Letrozole + HP

Arm description:

Palbociclib 125 mg/day orally for 21 days then 7 days rest, for 4 28-day cycles
Letrozole 2.5 mg/day orally for 16 weeks

Trastuzumab 600 mg sc every 3 weeks for 5 doses
Pertuzumab 840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses

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

Dosage and administration details:

125 mg/day orally for 21 days then 7 days rest, for 4 28-day cycles

Investigational medicinal product name	Letrozole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg/day orally for 16 weeks

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg sc every 3 weeks for 5 doses

Investigational medicinal product name	Pertuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses

Number of subjects in period 1	Paclitaxel + HP	Palbociclib + Letrozole + HP
Started	74	73
Completed	73	72
Not completed	1	1
Consent withdrawn by subject	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Paclitaxel + HP
Reporting group description:	
Paclitaxel 80 mg/m2 iv on day 1,8,15 every 28 days for 4 cycles Trastuzumab 600 mg sc every 3 weeks for 5 doses Pertuzumab 840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses	
Reporting group title	Palbociclib + Letrozole + HP
Reporting group description:	
Palbociclib 125 mg/day orally for 21 days then 7 days rest, for 4 28-day cycles Letrozole 2.5 mg/day orally for 16 weeks Trastuzumab 600 mg sc every 3 weeks for 5 doses Pertuzumab 840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses	

Reporting group values	Paclitaxel + HP	Palbociclib + Letrozole + HP	Total
Number of subjects	74	73	147
Age categorical Units: Subjects			
Adults (18-64 years)	21	25	46
From 65-84 years	52	48	100
85 years and over	1	0	1
Gender categorical Units: Subjects			
Female	74	73	147
Male	0	0	0

Subject analysis sets	
Subject analysis set title	Treatment Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Out of 147 randomized patients 2 patients have not started any protocol treatment.	

Reporting group values	Treatment Population		
Number of subjects	145		
Age categorical Units: Subjects			
Adults (18-64 years)	46		
From 65-84 years	99		
85 years and over	1		
Gender categorical Units: Subjects			
Female	145		
Male	0		

End points

End points reporting groups

Reporting group title	Paclitaxel + HP

Reporting group description:

Paclitaxel 80 mg/m2 iv on day 1,8,15 every 28 days for 4 cycles
Trastuzumab 600 mg sc every 3 weeks for 5 doses
Pertuzumab 840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses

Reporting group title	Palbociclib + Letrozole + HP

Reporting group description:

Palbociclib 125 mg/day orally for 21 days then 7 days rest, for 4 28-day cycles
Letrozole 2.5 mg/day orally for 16 weeks
Trastuzumab 600 mg sc every 3 weeks for 5 doses
Pertuzumab 840 mg iv loading dose, then 420 mg iv every 3 weeks for 5 doses

Subject analysis set title	Treatment Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Out of 147 randomized patients 2 patients have not started any protocol treatment.

Primary: Pathological Complete Response (pCR)

End point title	Pathological Complete Response (pCR)[1]

End point description:

Pathological complete response pCR, defined as absence of invasive tumor cells in the breast and in the axillary lymph nodes at the time of surgery (ypT0/ypTis ypN0).

End point type	Primary

End point timeframe:

Assessed within 30 days of the time of breast surgery after completion of a treatment period of up to 16 weeks; up to 21 weeks. If the patient does not undergo surgery, assessment will occur within 30 days after all treatment is stopped; up to 30 weeks.

Notes:

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

End point values	Paclitaxel + HP	Palbociclib + Letrozole + HP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants	24	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Pathological Complete Response (pCR) in the breast

End point title	Pathological Complete Response (pCR) in the breast

End point description:

Defined as the absence of invasive tumour cells in the breast at the time of surgery (ypT0/ypTis) determined from the local histopathologic evaluation according to the American Joint Committee on Cancer Staging Manual.

End point type	Secondary

End point timeframe:

Assessed within 30 days of the time of breast surgery after completion of a treatment period of up to 16 weeks; up to 21 weeks. If the patient does not undergo surgery, assessment will occur within 30 days after all treatment is stopped; up to 30 weeks.

End point values	Paclitaxel + HP	Palbociclib + Letrozole + HP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants	26	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response

End point title	Objective Response

End point description:

The number of patients with partial or complete response measured physically by caliper and by ultrasound and mammography. Response was assessed using World Health Organization tumor measurement and response criteria.

Complete response (CR) - The disappearance of all known disease. Partial response (PR) - A 50% or more decrease in total tumor size, i.e., the sum of the products of the maximal diameter (MD) and the corresponding largest perpendicular diameter (LPD) of the lesions which have been measured to determine the effect of therapy. In addition, there can be no appearance of new lesions or progression of any lesion.

Stable disease (SD) - Neither a 50% decrease in total tumor size, nor a 25% increase in the size of one or more measurable lesions has been determined.

Progressive disease (PD) - An increase of least 25% in total tumor size relative to the smallest size measured during the trial

End point type	Secondary

End point timeframe:

Tumor assessments were performed by ultrasound and mammography at screening (prior to treatment start), and before surgery; measurements by caliper were assessed at the same time points and at the end of cycle 2 (28 days/cycle), approximately 56 days.

End point values	Paclitaxel + HP	Palbociclib + Letrozole + HP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants				
Objective response - complete response	35	38		
Objective response - partial response	17	19		
Objective response - stable disease	4	4		
Objective response - progressive disease	3	2		

Objective response - not evaluable	14	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Breast Conserving Surgery (BCS)

End point title	Rate of Breast Conserving Surgery (BCS)

End point description:

Defined as the number of patients undergoing BCS, divided by the number of patients in the assessable population (subset of the randomized population with RBsig status successfully determined who received at least 1 dose of medication).

End point type	Secondary

End point timeframe:

From randomization until completion of study, up to 20 months

End point values	Paclitaxel + HP	Palbociclib + Letrozole + HP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	72		
Units: Participants	49	59		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessed at the end of every 4-week cycle until the end of trial treatment prior to surgery; up to 20 weeks. Only serious adverse events were assessed 30 days after end of treatment; up to 21 weeks.

Adverse event reporting additional description:

The severity and causality will be classified according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 5. The CTCAE is available for downloading on the internet at http://evs.nci.nih.gov/ftp1/CTCAE/About.html. For this trial, Grade 1s were not collected for non-targeted adverse events and hence

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	5

Reporting groups

Reporting group title	Paclitaxel + HP
Reporting group description: -	
Reporting group title	Palbociclib + Letrozole + HP

Reporting group description: -

Serious adverse events	Paclitaxel + HP	Palbociclib + Letrozole + HP	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 73 (31.51%)	39 / 72 (54.17%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 73 (2.74%)	4 / 72 (5.56%)	
occurrences causally related to treatment / all	2 / 2	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (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			
Pneumonitis			

subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	5 / 73 (6.85%)	31 / 72 (43.06%)	
occurrences causally related to treatment / all	6 / 6	66 / 66	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 73 (1.37%)	3 / 72 (4.17%)	
occurrences causally related to treatment / all	1 / 1	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 73 (1.37%)	3 / 72 (4.17%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell decreased			
subjects affected / exposed	1 / 73 (1.37%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Left ventricular systolic dysfunction			

subjects affected / exposed	1 / 73 (1.37%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Eye disorders - Other, specify			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	8 / 73 (10.96%)	6 / 72 (8.33%)	
occurrences causally related to treatment / all	10 / 11	8 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal obstruction			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin and cutaneous disorders			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alopecia			

subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (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			
Infections			
subjects affected / exposed	0 / 73 (0.00%)	2 / 72 (2.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalemia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle cramp			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Paclitaxel + HP	Palbociclib + Letrozole + HP	
Total subjects affected by non-serious adverse events subjects affected / exposed	68 / 73 (93.15%)	69 / 72 (95.83%)	
Vascular disorders Thromboembolic event subjects affected / exposed occurrences (all)	2 / 73 (2.74%) 2	1 / 72 (1.39%) 2	
Hypertension subjects affected / exposed occurrences (all)	7 / 73 (9.59%) 18	1 / 72 (1.39%) 3	
Phlebitis subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1	0 / 72 (0.00%) 0	
Hot flashes subjects affected / exposed occurrences (all)	0 / 73 (0.00%) 0	1 / 72 (1.39%) 3	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	8 / 73 (10.96%) 13	2 / 72 (2.78%) 2	
Immune system disorders Allergic reaction subjects affected / exposed occurrences (all)	8 / 73 (10.96%) 11	0 / 72 (0.00%) 0	
Reproductive system and breast disorders Vaginal dryness subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1	0 / 72 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1	0 / 72 (0.00%) 0	
Epistaxis subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1	0 / 72 (0.00%) 0	
Hypoxia			

subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	12 / 73 (16.44%)	23 / 72 (31.94%)	
occurrences (all)	23	119	
Platelet count decreased			
subjects affected / exposed	2 / 73 (2.74%)	28 / 72 (38.89%)	
occurrences (all)	5	66	
Ejection fraction decreased			
subjects affected / exposed	4 / 73 (5.48%)	2 / 72 (2.78%)	
occurrences (all)	4	2	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 73 (1.37%)	3 / 72 (4.17%)	
occurrences (all)	3	5	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 73 (0.00%)	2 / 72 (2.78%)	
occurrences (all)	0	3	
White blood cell decreased			
subjects affected / exposed	1 / 73 (1.37%)	3 / 72 (4.17%)	
occurrences (all)	2	4	
Conjunctivitis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	2	
GGT increased			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Weight loss			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Infusion related reaction			
subjects affected / exposed	6 / 73 (8.22%)	0 / 72 (0.00%)	
occurrences (all)	8	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	5 / 73 (6.85%)	0 / 72 (0.00%)	
occurrences (all)	9	0	
Dysgeusia			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	36 / 73 (49.32%)	35 / 72 (48.61%)	
occurrences (all)	115	120	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	19 / 73 (26.03%)	16 / 72 (22.22%)	
occurrences (all)	39	24	
Diarrhea			
subjects affected / exposed	45 / 73 (61.64%)	47 / 72 (65.28%)	
occurrences (all)	125	142	
Abdominal pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Mucositis oral			
subjects affected / exposed	1 / 73 (1.37%)	4 / 72 (5.56%)	
occurrences (all)	1	6	

Stomach pain			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Anal fissure			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Anal mucositis			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 73 (0.00%)	2 / 72 (2.78%)	
occurrences (all)	0	4	
Vomiting			
subjects affected / exposed	0 / 73 (0.00%)	1 / 72 (1.39%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatobiliary disorder			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	4	0	
Skin and subcutaneous tissue disorders			
Skin and cutaneous disorders			
subjects affected / exposed	30 / 73 (41.10%)	22 / 72 (30.56%)	
occurrences (all)	75	57	
Alopecia			
subjects affected / exposed	3 / 73 (4.11%)	1 / 72 (1.39%)	
occurrences (all)	7	1	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 72 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Infections			
subjects affected / exposed	18 / 73 (24.66%)	14 / 72 (19.44%)	
occurrences (all)	26	23	
Metabolism and nutrition disorders			

Hypoalbuminemia subjects affected / exposed occurrences (all)	1 / 73 (1.37%) 1	0 / 72 (0.00%) 0	
Hypokalemia subjects affected / exposed occurrences (all)	0 / 73 (0.00%) 0	1 / 72 (1.39%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2020	Given the important benefit brought by CDK4/6 inhibitors that has been confirmed in metastatic setting and which is expected in earlier stages, as suggested for example by first results of the CORALEEN study (Lancet Oncol 2020), the protocol has been updated to relax the eligibility criteria, now expanded from elderly (aged 65) to postmenopausal patients. This will help accelerating the accrual to yield sooner relevant and important data highly expected. In addition, the safety information for palbociclib has been updated based on the latest version of the SmPC (dated 19 December 2019) to account for the new safety risk of interstitial lung disease (ILD). ILD and pneumonitis have been added to the list of targeted adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported