



Clinical trial results:

An Open-label, Randomized, Non-comparative Phase 2 Study of ARV-471 or Anastrozole in Post-menopausal Women With ER+/HER2- Breast Cancer in the Neoadjuvant Setting

Summary

EudraCT number	2021-005081-17
Trial protocol	DE ES
Global end of trial date	25 July 2024

Results information

Result version number	v1 (current)
This version publication date	23 July 2025
First version publication date	23 July 2025

Trial information

Trial identification

Sponsor protocol code	ARV-471-BC-201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05549505
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Arvinas Estrogen Receptor, Inc (Arvinas)
Sponsor organisation address	5 Science Park 395 Winchester Avenue New Haven, Connecticut, United States, 06511
Public contact	Clinical Trials Information Desk, Arvinas Estrogen Receptor, Inc., clinicaltrialinformationdesk@arvinas.com
Scientific contact	Clinical Trials Information Desk, Arvinas Estrogen Receptor, Inc., clinicaltrialinformationdesk@arvinas.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	25 July 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main goal of this study was to evaluate the biological and clinical activity of vepdegestrant and anastrozole, respectively, in participants with ER+/HER2- breast cancer amenable to definitive surgical resection.

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles derived from international guidelines including the Declaration of Helsinki, CIOMS International Ethical Guidelines, applicable ICH GCP Guidelines and other applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 2023
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	Spain: 100
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Georgia: 18
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	152
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)	67

From 65 to 84 years	83
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 152 participants were enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: ARV-471 (Experimental)

Arm description:

Participants received 200 mg ARV-471 (2*100 mg tablets) once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).

Arm type	Experimental
Investigational medicinal product name	ARV-471
Investigational medicinal product code	
Other name	Vepdegestrant, PF-07850327
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg ARV-471 (2*100 mg tablets) once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).

Arm title	Arm B: Anastrozole
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Arm description:

Participants received 1 mg Anastrozole tablet orally once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).

Arm type	Active comparator
Investigational medicinal product name	Anastrozole
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

1 mg Anastrozole tablet once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).

Number of subjects in period 1	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole
Started	102	50
Treated	101	48
Completed	94	41
Not completed	8	9
Consent withdrawn by subject	3	3
Other: Miscellaneous	3	6
Lost to follow-up	2	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A: ARV-471 (Experimental)
Reporting group description:	
Participants received 200 mg ARV-471 (2*100 mg tablets) once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).	
Reporting group title	Arm B: Anastrozole
Reporting group description:	
Participants received 1 mg Anastrozole tablet orally once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).	

Reporting group values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole	Total
Number of subjects	102	50	152
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	67.4	66.8	
standard deviation	± 9.23	± 8.31	-
Gender categorical			
Units: Subjects			
Female	102	50	152
Male	0	0	0
Race			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	3
White	98	46	144
Unknown or Not Reported	2	0	2
Other	0	1	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	38	23	61
Not Hispanic or Latino	59	25	84
Unknown or Not Reported	5	2	7
Percentage of Tumor Cells Positive for Ki-67			
Measure Description: Ki-67 expression assessed by immunohistochemical staining in a central laboratory.			
Measure Analysis Population Description: Only participants with evaluable central Ki-67 results included in the analysis, which was 100 participants for Arm A: ARV-471 (Experimental) and 48 participants for Arm B: Anastrozole (Active Control).			
Units: Percentage of tumor cells with Ki67			
arithmetic mean	20.6	20.1	

standard deviation	± 14.01	± 12.25	-
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End points

End points reporting groups

Reporting group title	Arm A: ARV-471 (Experimental)
Reporting group description:	
Participants received 200 mg ARV-471 (2*100 mg tablets) once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).	
Reporting group title	Arm B: Anastrozole
Reporting group description:	
Participants received 1 mg Anastrozole tablet orally once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).	

Primary: Percent Reduction in Ki-67 Expression From Baseline to Day 15 in Tumor Biopsies

End point title	Percent Reduction in Ki-67 Expression From Baseline to Day 15 in Tumor Biopsies ^[1]
End point description:	
Tumor biopsy Ki-67 expression (% of tumor cells positive for Ki-67) at baseline and Cycle 1 Day 15 (C1D15) collected. Ki-67 expression assessed by immunohistochemical staining in a central laboratory. Log-transformed Ki-67 after 2 weeks of treatment as percentage of baseline value, ie, ratio between Ki-67 measurements from C1D15 visit and baseline was modelled by a generalized linear model (GLM) with baseline Ki-67 score and tumor size and treatment as co-variables. Treatment effects back transformed into geometric means and Confidence Intervals. Percent change/relative reduction, of Ki-67, 2 weeks post treatment were reported as complement of ratio between Ki-67 measurement from C1D15 and baseline, i.e. $100\% \times (1 - \text{Ki-67 from C1D15} / \text{Ki-67 from baseline})$. Ki-67 Evaluable Set = all enrolled/randomised participants receiving at least one dose of study treatment with evaluable central Ki-67 measurements other than '0' or '< 1' from baseline and evaluable Ki-67 measurements from C1D15 visits.	
End point type	Primary
End point timeframe:	
Baseline (during screening, prior to Day 1) and Day 15	
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: Per protocol, no formal comparisons between vepdegestrant and anastrozole or hypotheses testing were planned for this study.	

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	46		
Units: percent reduction				
number (confidence interval 95%)	71.4 (60.6 to 79.3)	72.9 (57.8 to 82.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Study Drug Discontinuation

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs and TEAEs Leading to Study Drug Discontinuation
End point description: An AE is any untoward medical occurrence in a participant, temporally associated with use of study intervention, whether or not considered related to the it. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention. A serious adverse event (SAE) was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. A TEAE is an AE that emerges or worsens on/after the first dose of ARV-471/Anastrozole to 30 days after the last administration of the study intervention (ie, study drug treatment or surgical resection, whichever occurs last). Safety Analysis Set consisting of all enrolled participants who received at least 1 dose of study intervention.	
End point type	Secondary
End point timeframe: From signing of consent to minimum of 30 days after last administration of study drug (up to approximately 6.5 months)	

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	48		
Units: participants				
TEAEs	82	37		
Serious TEAEs	4	5		
TEAEs leading to study drug discontinuation	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Pathologic Stage at the Time of Surgical Resection

End point title	Pathologic Stage at the Time of Surgical Resection
End point description: Local pathological assessment of the tissue from surgical resection (performed after approximately 5.5 months of treatment), at minimum, included pathologic stage (ypT and ypN stage) as described in the Statistical Analysis Plan (SAP). The number of participants with the following disease staging at post-surgery are summarized: Pathologic Tumor - ypT (ypTx, ypT0, ypTis, ypT1mi, ypT1a, ypT1b, ypT1c, ypT2, ypT3, ypT4a, ypT4b, ypT4c) Pathological Lymph Nodes - ypN (ypNX, ypN0, ypN0[i+], ypN0[mol+], ypN1, ypN1mi, ypN1a, ypN1b, ypN1c, ypN2, ypN2a, ypN2b, ypN3, ypN3a, ypN3b, ypN3c). Full Analysis Set included all the enrolled participants who were randomized.	
End point type	Secondary
End point timeframe: At Cycle 6 Day 18 (approximately 5.5 months), each cycle is 28 days	

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: participants				
Pathologic Tumor ypTx	0	0		
Pathologic Tumor ypT0	1	0		
Pathologic Tumor ypTis	1	0		
Pathologic Tumor ypT1mi	1	0		
Pathologic Tumor ypT1a	6	1		
Pathologic Tumor ypT1b	7	2		
Pathologic Tumor ypT1c	36	14		
Pathologic Tumor ypT2	33	21		
Pathologic Tumor ypT3	4	2		
Pathologic Tumor ypT4a	1	0		
Pathologic Tumor ypT4b	0	0		
Pathologic Tumor ypT4c	0	0		
Pathologic Tumor Not Evaluable	12	10		
Pathological Lymph Nodes ypNX	0	0		
Pathological Lymph Nodes ypN0	51	20		
Pathological Lymph Nodes ypN0(i+)	0	0		
Pathological Lymph Nodes ypN1	5	4		
Pathological Lymph Nodes ypN0(mol+)	0	0		
Pathological Lymph Nodes ypN1mi	4	3		
Pathological Lymph Nodes ypN1a	21	6		
Pathological Lymph Nodes ypN1b	0	0		
Pathological Lymph Nodes ypN1c	1	0		
Pathological Lymph Nodes ypN2	2	2		
Pathological Lymph Nodes ypN2a	3	4		
Pathological Lymph Nodes ypN2b	0	0		
Pathological Lymph Nodes ypN3	0	0		
Pathological Lymph Nodes ypN3a	3	1		
Pathological Lymph Nodes ypN3b	0	0		
Pathological Lymph Nodes ypN3c	0	0		
Pathological Lymph Nodes Not evaluable	12	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Pathological Complete Response (pCR) Rate at the Time of Surgical Resection

End point title	Pathological Complete Response (pCR) Rate at the Time of Surgical Resection
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End point description:

pCR is defined as no invasive cancer in the breast and sampled axillary lymph nodes following completion of neoadjuvant systemic therapy (ie, Pathologic Tumor - ypT = ypT0 or ypTis, and Pathologic Lymph Nodes – ypN = ypN0 in the current AJCC staging system). pCR rate is the percentage of participants with pCR. Full Analysis set included all the enrolled participants who were randomized.

End point type	Secondary
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End point timeframe:

At Cycle 6 Day 18 (approximately 5.5 months), each cycle is 28 days

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: percentage of participants	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Modified Preoperative Endocrine Prognostic Index (mPEPI) Score of 0 at the Time of Surgical Resection

End point title	Number of Participants With Modified Preoperative Endocrine Prognostic Index (mPEPI) Score of 0 at the Time of Surgical Resection
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End point description:

mPEPI score was derived from factors assigned a numerical score following Neoadjuvant endocrine treatment (NET). Total mPEPI score assigned to each patient was the sum of the risk points derived from the pathological (pT) stage, lymph node (pN) stage and Ki67 level. Number of participants with score 0 was reported. Participants with mPEPI score of 0 have pathological stage pT1 or pT2, negative lymph nodes pN0 and proliferation index [Ki-67] of less than or equal to 2.7%. Full Analysis Set included all the enrolled participants who were randomized.

End point type	Secondary
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End point timeframe:

At Cycle 6 Day 18 (approximately 5.5 months), each cycle is 28 days

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: participants	21	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Breast Conserving Surgery (BCS) Rate

End point title	Breast Conserving Surgery (BCS) Rate
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End point description:

Breast conserving surgery (BCS) Rate is the percentage of participants received breast conserving surgery. Full Analysis Set included all the enrolled participants who were randomized.

End point type	Secondary
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End point timeframe:

At Cycle 6 (from Day 141 to Day 168), each cycle is 28 days

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: percentage of participants				
number (confidence interval 95%)	69.6 (60.1 to 77.7)	54.0 (40.4 to 67.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic Response Per Modified Response Evaluation Criteria in Solid Tumors (mRECIST) in Primary Tumor During Cycle 6

End point title	Radiographic Response Per Modified Response Evaluation Criteria in Solid Tumors (mRECIST) in Primary Tumor During Cycle 6
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End point description:

The number of participants with Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Not Evaluable (NE) per mRECIST calculated. CR = disappearance of all target lesions, PR is $\geq 30\%$ decrease in sum of diameters of target lesions, progressive disease (PD) is $\geq 20\%$ increase in sum of diameters of target lesions, stable disease (SD) is $< 30\%$ decrease or $< 20\%$ increase in sum of diameters of target lesions. Full Analysis Set included all the enrolled participants who were randomized.

End point type	Secondary
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End point timeframe:

At Cycle 6 (from Day 141 to Day 168), each cycle is 28 days

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	50		
Units: participants				
CR	5	4		
PR	37	17		
Stable Disease	38	16		
Progressive disease	3	1		
NE	19	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline at Cycle 6 Day 1 in Caliper Measurement of the Primary Tumor

End point title	Percentage Change From Baseline at Cycle 6 Day 1 in Caliper Measurement of the Primary Tumor
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End point description:

The percentage change from the baseline of the primary breast tumor size in physical exam calculated in caliper measurement. Caliper-based response is the maximum percentage decrease or minimum percentage increase if there is no decrease per participant. Here 'Number of subjects analyzed' signifies those participants who were evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Baseline (Day 1) and Cycle 6 Day 1 (At Day 141), each cycle is 28 days

End point values	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	19		
Units: percent change				
arithmetic mean (standard deviation)	-32.35 ($\pm$ 23.739)	-42.88 ($\pm$ 18.041)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first study drug administration up to approximately 6.5 months

Adverse event reporting additional description:

Safety Analysis Set consisting of all enrolled participants who received at least 1 dose of study intervention.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Arm A: ARV-471 (Experimental)
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Reporting group description:

Participants received 200 mg ARV-471 (2*100 mg tablets) once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).

Reporting group title	Arm B: Anastrozole
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Reporting group description:

Participants received 1 mg Anastrozole tablet orally once daily for approximately 5.5 months prior to undergoing surgical resection (no later than C6D18 + 14 days).

Serious adverse events	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 101 (3.96%)	5 / 48 (10.42%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Post procedural haematoma			
subjects affected / exposed	0 / 101 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 101 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	0 / 101 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 101 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status change			
subjects affected / exposed	1 / 101 (0.99%)	0 / 48 (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			
Bacteraemia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 101 (0.99%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 48 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 101 (0.00%)	1 / 48 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyelonephritis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 48 (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	Arm A: ARV-471 (Experimental)	Arm B: Anastrozole	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 101 (71.29%)	32 / 48 (66.67%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 101 (5.94%)	1 / 48 (2.08%)	
occurrences (all)	6	1	
Vascular disorders			
Hot flush			
subjects affected / exposed	25 / 101 (24.75%)	10 / 48 (20.83%)	
occurrences (all)	28	10	
Hypertension			
subjects affected / exposed	12 / 101 (11.88%)	4 / 48 (8.33%)	
occurrences (all)	18	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 101 (4.95%)	3 / 48 (6.25%)	
occurrences (all)	5	3	
Headache			
subjects affected / exposed	8 / 101 (7.92%)	1 / 48 (2.08%)	
occurrences (all)	10	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 101 (0.99%)	3 / 48 (6.25%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	21 / 101 (20.79%)	5 / 48 (10.42%)	
occurrences (all)	24	5	
Fatigue			

subjects affected / exposed occurrences (all)	13 / 101 (12.87%) 14	3 / 48 (6.25%) 3	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	7 / 101 (6.93%) 7	2 / 48 (4.17%) 2	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	16 / 101 (15.84%) 19 15 / 101 (14.85%) 16	3 / 48 (6.25%) 3 1 / 48 (2.08%) 2	
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 101 (0.99%) 1	3 / 48 (6.25%) 3	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	9 / 101 (8.91%) 10	1 / 48 (2.08%) 1	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	14 / 101 (13.86%) 16	15 / 48 (31.25%) 15	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	6 / 101 (5.94%) 6 4 / 101 (3.96%) 4 8 / 101 (7.92%) 10	1 / 48 (2.08%) 1 3 / 48 (6.25%) 3 1 / 48 (2.08%) 1	
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	8 / 101 (7.92%) 10	0 / 48 (0.00%) 0	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2023	- Surgical resection accepted C6D18 ± 14 days instead of C6D18 ± 10 days - If screening ECG is used for C1D1, it must be done in triplicate and on a vendor machine - Study drug may be continued beyond C6D18 + 14 days if surgical resection is delayed for non-study related reasons and after discussion with medical monitor. - Added MRI as preferred imaging modality in Radiographic Imaging Assessment - Addition of definition of last administration of study intervention as study drug treatment or surgical resection, whichever comes last. - Clarification that radiographic response will be evaluated per mRECIST. - Inclusion criteria clarified to participants for whom neoadjuvant endocrine monotherapy is deemed appropriate. - Exclusion criteria now to exclude patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported