

**Clinical trial results:****A Phase 1b/2 Randomized Study of MEDI-573 in Combination with an Aromatase Inhibitor (AI) Versus AI Alone in Women with Metastatic Breast Cancer (MBC)****Summary**

EudraCT number	2011-000198-29
Trial protocol	ES DE HU BE GB
Global end of trial date	28 June 2019

**Results information**

Result version number	v1 (current)
This version publication date	14 June 2020
First version publication date	14 June 2020

**Trial information****Trial identification**

Sponsor protocol code	CD-ON-MEDI-573-1030
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01446159
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	Mohammed Dar, One MedImmune Way, +1 301-398-1894, information.center@astrazeneca.com
Scientific contact	Mohammed Dar, MedImmune, LLC, +1 301-398-1894, information.center@astrazeneca.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	20 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2019
Global end of trial reached?	Yes
Global end of trial date	28 June 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the safety and tolerability of 3 dose levels of MEDI-573 in combination with an AI in participants with HR+, HER2-negative MBC.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United States: 99
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Israel: 19
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Belgium: 22
Worldwide total number of subjects	183
EEA total number of subjects	56

Notes:

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**Subjects enrolled per age group**

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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)	96
From 65 to 84 years	84
85 years and over	3

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## Subject disposition

### Recruitment

Recruitment details:

The study was conducted across 10 countries (Belgium, Canada, France, Germany, Hungary, Israel, Spain, Poland, United Kingdom, USA).

### Pre-assignment

Screening details:

A total of 187 participants were screened in the study. Of which, 183 participants were treated with study drugs.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)

Arm description:

Participants enrolled in Phase 1b of the study and received intravenous infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle and AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

Arm type	Experimental
Investigational medicinal product name	MEDI-573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

Investigational medicinal product name	Aromatase inhibitor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

<b>Arm title</b>	MEDI-573 30 mg/kg + AI
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Arm description:

Participants enrolled in Phase 1 b of the study and received intravenous infusion of MEDI-573 30 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

Arm type	Experimental
Investigational medicinal product name	Aromatase inhibitor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:	
AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Investigational medicinal product name	MEDI-573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
IV infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
<b>Arm title</b>	MEDI-573 45 mg/kg + AI

Arm description:	
Participants received intravenous infusion of MEDI-573 45 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons. Three participants were enrolled in Phase 1b and 89 were enrolled in Phase 2 of the study.	
Arm type	Experimental
Investigational medicinal product name	MEDI-573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
IV infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Investigational medicinal product name	Aromatase inhibitor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:	
AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
<b>Arm title</b>	Aromatase Inhibitor

Arm description:	
Participants enrolled in Phase 2 of the study and received oral AI (letrozole, anastrozole, or exemestane) once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Arm type	Active comparator
Investigational medicinal product name	Aromatase Inhibitor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:	
aromatase inhibitor	

Number of subjects in period 1	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI
	Started	3	3
Completed	0	0	21
Not completed	3	3	71
Adverse event, serious fatal	2	3	43
Consent withdrawn by subject	1	-	14
Not specified	-	-	13
Lost to follow-up	-	-	1

Number of subjects in period 1	Aromatase Inhibitor
Started	85
Completed	23
Not completed	62
Adverse event, serious fatal	36
Consent withdrawn by subject	11
Not specified	13
Lost to follow-up	2

## Baseline characteristics

### Reporting groups

Reporting group title	MEDI-573 10 mg/kg + aromatase inhibitor (AI)
Reporting group description: Participants enrolled in Phase 1b of the study and received intravenous infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle and AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Reporting group title	MEDI-573 30 mg/kg + AI
Reporting group description: Participants enrolled in Phase 1 b of the study and received intravenous infusion of MEDI-573 30 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Reporting group title	MEDI-573 45 mg/kg + AI
Reporting group description: Participants received intravenous infusion of MEDI-573 45 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons. Three participants were enrolled in Phase 1b and 89 were enrolled in Phase 2 of the study.	
Reporting group title	Aromatase Inhibitor
Reporting group description: Participants enrolled in Phase 2 of the study and received oral AI (letrozole, anastrozole, or exemestane) once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	

Reporting group values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI
Number of subjects	3	3	92
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	1	49
From 65-84 years	1	2	41
85 years and over	0	0	2
Age Continuous Units: Years			
arithmetic mean	66.3	61.0	63.2
standard deviation	± 12.3	± 8.7	± 10.5
Sex: Female, Male Units: Participants			
Female	3	3	92
Male	0	0	0

Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	6
White	2	3	84
More than one race	0	0	0
Unknown or Not Reported	0	0	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	0	7
Not Hispanic or Latino	3	3	85
Unknown or Not Reported	0	0	0

Reporting group values	Aromatase Inhibitor	Total	
Number of subjects	85	183	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	44	96	
From 65-84 years	40	84	
85 years and over	1	3	
Age Continuous			
Units: Years			
arithmetic mean	63.3		
standard deviation	± 11.0	-	
Sex: Female, Male			
Units: Participants			
Female	85	183	
Male	0	0	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	8	
White	82	171	
More than one race	0	0	
Unknown or Not Reported	1	3	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	6	13	
Not Hispanic or Latino	79	170	

Unknown or Not Reported	0	0	
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## End points

### End points reporting groups

Reporting group title	MEDI-573 10 mg/kg + aromatase inhibitor (AI)
Reporting group description: Participants enrolled in Phase 1b of the study and received intravenous infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle and AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Reporting group title	MEDI-573 30 mg/kg + AI
Reporting group description: Participants enrolled in Phase 1 b of the study and received intravenous infusion of MEDI-573 30 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	
Reporting group title	MEDI-573 45 mg/kg + AI
Reporting group description: Participants received intravenous infusion of MEDI-573 45 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons. Three participants were enrolled in Phase 1b and 89 were enrolled in Phase 2 of the study.	
Reporting group title	Aromatase Inhibitor
Reporting group description: Participants enrolled in Phase 2 of the study and received oral AI (letrozole, anastrozole, or exemestane) once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.	

### Primary: Phase 1b and Phase 2: Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Phase 1b and Phase 2: Number of Participants with Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) <sup>[1]</sup>
End point description: An Adverse Event (AE) is any unfavourable and unintended sign, symptoms, or diseases temporally associated with use of study drug, whether or not considered related to study drug. A serious adverse event (SAE) is an AE that results in death, initial or prolonged inpatient hospitalization, life-threatening, persistent or significant disability/incapacity, congenital anomaly/birth defect, or an important medical event. TEAEs and TESAEs are defined as AEs and SAEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 60 days after the last study drug or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years). Safety population included all participants who received any study therapy and were analysed per the treatment they actually received was considered for this end point.	
End point type	Primary
End point timeframe: From the start of study treatment (Day 1) through 60 days after the last dose of treatment or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years)	

#### 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	92	85
Units: Participants				
Any TEAEs	3	3	90	82
Any TESAEs	2	0	21	16

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase 1b: Number of Participants with dose-limiting toxicities (DLTs)

End point title	Phase 1b: Number of Participants with dose-limiting toxicities (DLTs) <sup>[2][3]</sup>
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End point description:

The AEs that occurred during Cycle 1 (Days 1 to 21) and were suspected of having a causal relationship to MEDI-573 and were  $\geq$  Grade 3 in severity were considered as DLTs. Evaluable population included all participants in Phase 1b of the study, who received at least 1 full cycle of MEDI-573 and completed the safety follow-up through the DLT evaluation period (Days 1 to 21 of Cycle 1) was considered for this end point.

End point type	Primary
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End point timeframe:

Up to Day 21 of Cycle 1

Notes:

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

Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	3	
Units: Participants	0	0	0	

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase 1b: Number of DLTs

End point title	Phase 1b: Number of DLTs <sup>[4][5]</sup>
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End point description:

The AEs that occurred during Cycle 1 (Days 1 to 21) and were suspected of having a causal relationship to MEDI-573 and were  $\geq$  Grade 3 in severity were considered as DLTs. Evaluable population included all participants in Phase 1b of the study, who received at least 1 full cycle of MEDI-573 and completed the safety follow-up through the DLT evaluation period (Days 1 to 21 of Cycle 1) was considered for this end point.

End point type | Primary

End point timeframe:

Up to Day 21 of Cycle 1

Notes:

[4] - 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	3	
Units: DLT events	0	0	0	

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 2: Progression-free Survival (PFS)

End point title | Phase 2: Progression-free Survival (PFS)<sup>[6]</sup>

End point description:

Progression-free survival (PFS) was defined as the time from the randomization until the first documentation of disease progression or death due to any cause, whichever occurred first. The PFS was censored on the date of the last tumor assessment documenting absence of tumor progression for participants who had no documented progression and were still alive prior to data cut-off, dropout, or the initiation of alternate anticancer treatment. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1), as  $\geq 20\%$  increase in the sum of diameters of target lesions and an absolute increase in sum of diameters of  $\geq 5\text{mm}$  (compared to the previous minimum sum) or progression of non-target lesions or a new lesion. The Intent-to-Treat (ITT) population included all participants who enrolled in Phase 2 and received any study therapy and were analysed per their randomized treatment group was considered for this end point.

End point type | Primary

End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Months				
median (confidence interval 95%)	12.65 (8.15 to 15.54)	11.33 (8.54 to 15.54)		

### Statistical analyses

<b>Statistical analysis title</b>	Statistical analysis
Comparison groups	Aromatase Inhibitor v MEDI-573 45 mg/kg + AI
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.86
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.991
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.689
upper limit	1.429

### Secondary: Phase 1b and Phase 2: Number of Participants With Abnormal Clinical Laboratory Results Reported as TEAEs

End point title	Phase 1b and Phase 2: Number of Participants With Abnormal Clinical Laboratory Results Reported as TEAEs
End point description:	An abnormal laboratory finding which required an action or intervention by the investigator, or a finding judged by the investigator to represent a change beyond the range of normal physiologic fluctuation were reported as AEs. The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 60 days after the last study drug or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years). Safety population was considered for this end point.
End point type	Secondary
End point timeframe:	From the start of study treatment (Day 1) through 60 days after the last dose of treatment or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years)

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	92	85
Units: Participants				
Anemia	1	1	17	10
Eosinophilia	0	0	1	0
Leukopenia	0	0	0	3
Lymphopenia	0	0	1	2
Neutropenia	1	1	3	4
Pancytopenia	0	0	0	1
Thrombocytopenia	0	2	1	3
Granulocyte count decreased	0	1	0	0
Hemoglobin decreased	0	1	1	0
Lymphocyte count decreased	0	0	2	1
Monocyte count decreased	0	0	1	0
Neutrophil count decreased	0	0	2	0
Neutrophil count increased	0	0	1	0
Platelet count decreased	0	0	4	1
White blood cell count decreased	0	0	2	1
Alanine aminotransferase increased	2	0	8	4
Aspartate aminotransferase increased	2	1	6	4
Blood albumin decreased	0	0	1	0
Blood albumin increased	0	1	0	0
Blood alkaline phosphatase increased	0	1	5	5
Blood bicarbonate decreased	0	0	1	0
Blood bilirubin increased	0	0	0	1
Blood chloride decreased	0	0	1	0
Blood creatine increased	0	1	1	0
Blood creatinine decreased	0	0	0	1
Blood creatinine increased	0	1	8	2
Blood glucose increased	0	0	1	1
Blood lactate dehydrogenase increased	0	0	1	1
Blood magnesium decreased	0	1	0	0
Blood potassium decreased	0	0	1	0
Blood sodium decreased	0	1	0	0
Blood triglycerides increased	0	0	1	2
Blood urea increased	0	0	1	0
Blood uric acid increased	0	0	3	1
Gamma-glutamyl transferase decreased	0	1	0	0
Gamma-glutamyl transferase increased	1	1	9	4
Protein total decreased	0	1	0	1
Leukocytosis	0	0	0	1
Neutrophilia	0	0	1	0

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point title	Phase 1b and Phase 2: Number of Participants With Abnormal Vital Signs Reported as TEAEs
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End point description:

An abnormal vital signs that were judged by the investigator to be medically significant were reported as AEs. The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 60 days after the last study drug or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years). Safety population was considered for this end point.

End point type	Secondary
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End point timeframe:

From the start of study treatment (Day 1) through 60 days after the last dose of treatment or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years)

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	92	85
Units: Participants				
Bradycardia	1	0	1	1
Palpitations	1	0	1	2
Pyrexia	0	0	10	6
Temperature intolerance	0	0	1	1
Body temperature increased	0	0	1	0
Aspiration	0	0	1	0
Dyspnoea	2	0	18	14
Hypertension	0	0	8	13
Hypotension	1	0	1	0
Orthostatic hypotension	0	0	1	0

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Number of Participants with Abnormal Electrocardiogram (ECG) Reported as TEAEs

End point title	Phase 1b and Phase 2: Number of Participants with Abnormal Electrocardiogram (ECG) Reported as TEAEs
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End point description:

An abnormal ECG findings that were judged by the investigator to be medically significant were reported as AEs. The TEAEs are defined as AEs present at baseline that worsened in intensity after administration of study drug, or events absent at baseline that emerged after administration of study drug, up to 60 days after the last study drug or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years). Safety population was considered for this end point.

End point type	Secondary
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End point timeframe:

From the start of study treatment (Day 1) through 60 days after the last dose of treatment or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years)

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	92	85
Units: Participants				
Sinus bradycardia	1	0	2	0
Sinus tachycardia	0	0	0	1
Supraventricular tachycardia	0	0	0	2
Tachycardia	0	0	1	2
Angina pectoris	0	0	0	1
Arrhythmia	0	0	0	1
Atrial fibrillation	0	0	1	2
Atrial flutter	0	0	0	1
Atrioventricular block first degree	0	0	1	0
Bradycardia	1	0	1	1
Cardiac failure	0	0	1	0
Cardiac valve disease	0	0	1	0
Palpitation	1	0	1	2
Ventricular extrasystoles	0	0	1	0

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Number of Participants With Best Overall Tumor Response

End point title	Phase 2: Number of Participants With Best Overall Tumor Response <sup>[7]</sup>
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End point description:

Tumor evaluation was based on RECIST v1.1 by CT or MRI scan as: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR):  $\geq 30\%$  decrease in the sum of diameters of target lesions (compared to baseline) and no new lesions; Stable disease (SD): Neither sufficient shrinkage to qualify as a response nor sufficient growth to qualify as progression; Progressive Disease (PD):  $\geq 20\%$  increase in the sum of diameters of target lesions and an absolute increase in sum of diameters of  $\geq 5\text{mm}$  (compared to the previous minimum sum) or progression of non-target lesions or a new lesion; not evaluable (NE): either no or only a subset of lesion measurements are made at an assessment. Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type	Secondary
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End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those baseline period arms for which analysis was planned were reported in the end

point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Participants				
CR	1	2		
PR	23	21		
SD	48	46		
PD	15	12		
NE	2	4		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Objective Response Rate (ORR)

End point title	Phase 2: Objective Response Rate (ORR) <sup>[8]</sup>
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End point description:

The ORR was defined as percentage of participants with confirmed complete response or confirmed partial response, where CR was defined as disappearance of all target and non-target lesions and no new lesions and PR was defined as  $\geq 30\%$  decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type	Secondary
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End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Percentage of participants				
number (confidence interval 95%)	27.0 (18.1 to 37.4)	27.1 (18.0 to 37.8)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Time to Response

End point title	Phase 2: Time to Response <sup>[9]</sup>
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End point description:

Time to response was measured from treatment start to the first documentation of disease response and was evaluated only in participants who achieved objective response (confirmed CR or confirmed PR). The CR was defined as disappearance of all target and non-target lesions and no new lesions and PR was defined as  $\geq 30\%$  decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type	Secondary
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End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Months				
median (full range (min-max))	4.22 (1.7 to 18.0)	3.98 (1.9 to 16.8)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Duration of Response (DR)

End point title	Phase 2: Duration of Response (DR) <sup>[10]</sup>
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End point description:

Duration of response (DR) is measured from the first documentation of disease response to the first documented progressive disease and was evaluated only in participants who achieved objective response (confirmed CR or confirmed PR). The CR was defined as disappearance of all target and non-target lesions and no new lesions and PR was defined as  $\geq 30\%$  decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type	Secondary
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End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Months				
median (full range (min-max))	14.55 (4.5 to 58.8)	17.18 (2.1 to 45.1)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Time to Progression (TTP)

End point title	Phase 2: Time to Progression (TTP) <sup>[11]</sup>
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End point description:

Time to progression was measured from treatment start until the first documentation of disease progression. The PD was defined as  $\geq 20\%$  increase in the sum of diameters of TLs and an absolute increase in sum of diameters of  $\geq 5\text{mm}$  (compared to the previous minimum sum) or progression of non-target lesions or a new lesion. Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type	Secondary
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End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Months				
median (confidence interval 95%)	14.39 (8.34 to 18.69)	11.33 (8.54 to 17.97)		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Overall Survival (OS)

End point title	Phase 2: Overall Survival (OS) <sup>[12]</sup>
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End point description:

Overall survival (OS) was measured from treatment start until death. Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type	Secondary
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End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first

(Approximately 8 years)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Months				
median (full range (min-max))	39.39 (0.3 to 73.2)	38.34 (0.3 to 51.6)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Change in Tumor Size

End point title | Phase 2: Change in Tumor Size<sup>[13]</sup>

End point description:

Participants enrolled in Phase 2 and were the part of IIT population were analysed.

End point type | Secondary

End point timeframe:

From Day 1 until disease progression or death due to any cause, whichever occurred first (Approximately 8 years)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	85		
Units: Centimeters				
arithmetic mean (standard deviation)	-36.2 (± 35.8)	-26.8 (± 37.2)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Area Under the Serum Concentration-time Curve From Time Zero to Day 21 (AUC0-day21) of MEDI-573 for Cycle 1

End point title | Phase 1b and Phase 2: Area Under the Serum Concentration-time Curve From Time Zero to Day 21 (AUC0-day21) of MEDI-573 for Cycle 1<sup>[14]</sup>

End point description:

The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type Secondary

End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: µg·day/mL				
arithmetic mean (standard deviation)	1430 (± 867)	4500 (± 725)	7990 (± 1590)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Area Under the Serum Concentration-time Curve From Time Zero to Infinity (AUC0-inf) of MEDI-573 for Cycle 1

End point title Phase 1b and Phase 2: Area Under the Serum Concentration-time Curve From Time Zero to Infinity (AUC0-inf) of MEDI-573 for Cycle 1<sup>[15]</sup>

End point description:

The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type Secondary

End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: µg·day/mL				
arithmetic mean (standard deviation)	1500 (± 955)	4930 (± 691)	9570 (± 2310)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Dose-Normalised Area Under the Serum Concentration-time Curve From Time Zero to Infinity (DN AUC0-inf) of MEDI-573 for Cycle 1

End point title	Phase 1b and Phase 2: Dose-Normalised Area Under the Serum Concentration-time Curve From Time Zero to Infinity (DN AUC0-inf) of MEDI-573 for Cycle 1 <sup>[16]</sup>
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End point description:

The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type	Secondary
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End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: day·kg·µg/mL/mg				
arithmetic mean (standard deviation)	150 (± 95.5)	164 (± 23.0)	213 (± 51.3)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Maximum Observed Serum Concentration (Cmax) of MEDI-573 for Cycle 1

End point title	Phase 1b and Phase 2: Maximum Observed Serum Concentration (Cmax) of MEDI-573 for Cycle 1 <sup>[17]</sup>
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End point description:

The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type	Secondary
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End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: µg/mL				
arithmetic mean (standard deviation)	269 (± 74.1)	624 (± 210)	1070 (± 253)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Time to Reach Maximum Observed Serum Concentration (Tmax) of MEDI-573 for Cycle 1

End point title	Phase 1b and Phase 2: Time to Reach Maximum Observed Serum Concentration (Tmax) of MEDI-573 for Cycle 1 <sup>[18]</sup>
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End point description:

The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type	Secondary
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End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: Day				
median (full range (min-max))	0.04 (0 to 0.09)	0.07 (0.06 to 0.08)	0.07 (0.03 to 0.17)	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Systemic Clearance (CL) of MEDI-573 for Cycle 1

End point title	Phase 1b and Phase 2: Systemic Clearance (CL) of MEDI-573 for Cycle 1 <sup>[19]</sup>
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End point description:

The CL is a quantitative measure of the rate at which a drug substance is removed from the body. The total systemic clearance after intravenous dose was estimated by dividing the total administered dose by AUC(0-infinity). The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type	Secondary
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End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: mL/day/kg				
arithmetic mean (standard deviation)	8.29 (± 3.86)	6.17 (± 0.889)	4.96 (± 1.13)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Terminal Half life (t1/2) of MEDI-573 for Cycle 1

End point title	Phase 1b and Phase 2: Terminal Half life (t1/2) of MEDI-573 for Cycle 1 <sup>[20]</sup>
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End point description:

The elimination half-life (t1/2) is the time measured for the serum concentration of MEDI-573 to decrease by 1 half to its original concentration. The ITT population was considered for this analysis. Participants who received MEDI-573 were analysed.

End point type	Secondary
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End point timeframe:

Cycle 1 Days 1, 2, 8, 15, and 21 (Cycle 2 Day 1, pre-dose)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: Day				
arithmetic mean (standard deviation)	4.38 (± 1.07)	5.91 (± 2.09)	8.45 (± 2.23)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Concentration of insulin-like growth factor (IGF) I and IGF-II

End point title | Phase 1b and Phase 2: Concentration of insulin-like growth factor (IGF) I and IGF-II

End point description:

The mean concentration profiles of both IGF-I and IGF-II post administration of MEDI-573 in plasma were evaluated during treatment. Safety population was analysed for this end point. Participants with free IGF concentration were analysed. The "n" denotes the number of participants who were analysed for the specific endpoint. The arbitrary numbers "9999" signifies that standard deviation was not calculated as only one participant was evaluable for the specified arm.

End point type | Secondary

End point timeframe:

Baseline (Cycle1 Day1 pre-dose), end of treatment (EOT), and 60 days post last dose (Approximately 8 years)

End point values	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	Aromatase Inhibitor
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	92	85
Units: ng/mL				
arithmetic mean (standard deviation)				
Baseline Free IGF-I (n=3, 3, 82, 78)	2.57 (± 0.712)	1.25 (± 0.635)	3.49 (± 4.39)	1.89 (± 1.24)
Baseline Free IGF-II (n=3, 3, 84, 78)	3.81 (± 1.66)	3.07 (± 0.709)	3.01 (± 1.20)	3.03 (± 1.12)
EOT Free IGF-I (n=2, 2, 40, 38)	0.724 (± 0.421)	0.313 (± 0.0)	0.346 (± 0.130)	2.32 (± 3.64)
EOT Free IGF-II (n=2, 2, 40, 38)	0.625 (± 0.0)	0.625 (± 0.0)	0.641 (± 0.102)	3.12 (± 1.22)
60 days post last dose Free IGF-I (n=1, 2, 21, 22)	1.54 (± 99999)	1.33 (± 0.3)	1.02 (± 1.29)	4.62 (± 8.52)
60days post last dose Free IGF-II (n=1, 2, 21, 22)	1.49 (± 99999)	0.625 (± 0.0)	0.984 (± 0.734)	3.38 (± 1.51)

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1b and Phase 2: Number of participants With Positive Anti-drug Antibodies (ADA) to MEDI-573

End point title | Phase 1b and Phase 2: Number of participants With Positive Anti-drug Antibodies (ADA) to MEDI-573<sup>[21]</sup>

End point description:

Participants With Positive ADA to MEDI-573 are reported. Participants who received MEDI-573 and were analysed per the treatment they actually received were analysed for this outcome measure.

End point type | Secondary

End point timeframe:

Pre-infusion on Day 1 of each cycle, End of Treatment, Day 30, 60 and 90 post treatment (approximately 8 years)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

<b>End point values</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	92	
Units: Participants	0	0	1	

### **Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug (Day 1) through 60 days after the last dose of treatment or until the participants started another anticancer therapy, whichever occurs first (approximately 8 years)

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	MEDI-573 10 mg/kg + aromatase inhibitor (AI)
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Reporting group description:

Participants enrolled in Phase 1b of the study and received intravenous infusion of MEDI-573 10 mg/kg on Day 1 of each 21-day cycle and AI of the investigator's choice (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

Reporting group title	MEDI-573 30 mg/kg + AI
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Reporting group description:

Participants enrolled in Phase 1 b of the study and received intravenous infusion of MEDI-573 30 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

Reporting group title	MEDI-573 45 mg/kg + AI
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Reporting group description:

Participants received intravenous infusion of MEDI-573 45 mg/kg on Day 1 of each 21-day cycle and AI (letrozole, anastrozole, or exemestane) orally once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons. Three participants were enrolled in Phase 1b and 89 were enrolled in Phase 2 of the study.

Reporting group title	Aromatase Inhibitor
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Reporting group description:

Participants enrolled in Phase 2 of the study and received oral AI (letrozole, anastrozole, or exemestane) once daily until unacceptable toxicity, documentation of disease progression, or withdrawal for other reasons.

<b>Serious adverse events</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	21 / 92 (22.83%)
number of deaths (all causes)	2	3	43
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER METASTATIC			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
INTRADUCTAL PROLIFERATIVE BREAST LESION			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>LUNG ADENOCARCINOMA</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>OVARIAN CANCER METASTATIC</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>RECTAL NEOPLASM</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>UTERINE CANCER</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Vascular disorders</b>			
<b>EMBOLISM</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>HYPOTENSION</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>General disorders and administration site conditions</b>			
<b>CHEST PAIN</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PYREXIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
OVARIAN CYST			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ASPIRATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPHYSEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
MENTAL STATUS CHANGES			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>PSYCHOTIC DISORDER</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>SUICIDE ATTEMPT</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Injury, poisoning and procedural complications</b>			
<b>ACETABULUM FRACTURE</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>CERVICAL VERTEBRAL FRACTURE</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>SUBDURAL HAEMATOMA</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Cardiac disorders</b>			
<b>ATRIAL FIBRILLATION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>ATRIAL FLUTTER</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CARDIAC FAILURE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARTIAL SEIZURES			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER PERFORATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL MASS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 92 (3.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Hepatobiliary disorders</b>			
<b>BILIARY DILATATION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
<b>Renal and urinary disorders</b>			
<b>HYDRONEPHROSIS</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Musculoskeletal and connective tissue disorders</b>			
<b>BACK PAIN</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>FLANK PAIN</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>MUSCULOSKELETAL CHEST PAIN</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>PAIN IN EXTREMITY</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
<b>CELLULITIS</b>			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>DEVICE RELATED INFECTION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>DIVERTICULITIS</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>WOUND INFECTION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Metabolism and nutrition disorders</b>			
<b>DEHYDRATION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>HYPERGLYCAEMIA</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>HYPONATRAEMIA</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Aromatase Inhibitor		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 85 (18.82%)		
number of deaths (all causes)	36		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BREAST CANCER METASTATIC			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
INTRADUCTAL PROLIFERATIVE BREAST LESION			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LUNG ADENOCARCINOMA			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
OVARIAN CANCER METASTATIC			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RECTAL NEOPLASM			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
UTERINE CANCER			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
HYPOTENSION			

subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>General disorders and administration site conditions</b>			
<b>CHEST PAIN</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>PYREXIA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Reproductive system and breast disorders</b>			
<b>OVARIAN CYST</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>ASPIRATION</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>EMPHYSEMA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>PLEURAL EFFUSION</b>			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>PNEUMOTHORAX</b>			

subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>PULMONARY EMBOLISM</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Psychiatric disorders</b>			
<b>MENTAL STATUS CHANGES</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>PSYCHOTIC DISORDER</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>SUICIDE ATTEMPT</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Injury, poisoning and procedural complications</b>			
<b>ACETABULUM FRACTURE</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>CERVICAL VERTEBRAL FRACTURE</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>SUBDURAL HAEMATOMA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ATRIAL FLUTTER			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC FAILURE			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

PARTIAL SEIZURES			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIARRHOEA			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DYSPHAGIA			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTRIC ULCER PERFORATION			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTESTINAL MASS			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

PANCREATITIS ACUTE			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VOMITING			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
BILIARY DILATATION			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FLANK PAIN			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MUSCULOSKELETAL CHEST PAIN			

subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>PAIN IN EXTREMITY</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
<b>CELLULITIS</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>DEVICE RELATED INFECTION</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>DIVERTICULITIS</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>WOUND INFECTION</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>Metabolism and nutrition disorders</b>			
<b>DEHYDRATION</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>HYPERGLYCAEMIA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
<b>HYPONATRAEMIA</b>			

subjects affected / exposed	0 / 85 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	MEDI-573 10 mg/kg + aromatase inhibitor (AI)	MEDI-573 30 mg/kg + AI	MEDI-573 45 mg/kg + AI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	90 / 92 (97.83%)
<b>Vascular disorders</b>			
<b>HOT FLUSH</b>			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	13 / 92 (14.13%)
occurrences (all)	1	1	22
<b>HYPERTENSION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	8 / 92 (8.70%)
occurrences (all)	0	0	17
<b>PERIPHERAL COLDNESS</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
<b>General disorders and administration site conditions</b>			
<b>ASTHENIA</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	19 / 92 (20.65%)
occurrences (all)	1	0	33
<b>FATIGUE</b>			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	41 / 92 (44.57%)
occurrences (all)	3	6	96
<b>MUCOSAL INFLAMMATION</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	7 / 92 (7.61%)
occurrences (all)	0	0	9
<b>OEDEMA PERIPHERAL</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	9 / 92 (9.78%)
occurrences (all)	0	0	16
<b>PAIN</b>			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	2 / 92 (2.17%) 2
<b>PYREXIA</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	9 / 92 (9.78%) 11
<b>SWELLING</b> subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 92 (0.00%) 0
<b>Reproductive system and breast disorders</b> <b>ATROPHIC VULVOVAGINITIS</b> subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 92 (1.09%) 1
<b>BREAST HAEMORRHAGE</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 92 (0.00%) 0
<b>BREAST PAIN</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	4 / 92 (4.35%) 5
<b>Respiratory, thoracic and mediastinal disorders</b> <b>COUGH</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	19 / 92 (20.65%) 27
<b>DYSPNOEA</b> subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0	18 / 92 (19.57%) 21
<b>DYSPNOEA EXERTIONAL</b> subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	3 / 92 (3.26%) 7
<b>EPISTAXIS</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	5 / 92 (5.43%) 5
<b>OROPHARYNGEAL PAIN</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	6 / 92 (6.52%) 7
<b>Psychiatric disorders</b>			

ANXIETY			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	10 / 92 (10.87%)
occurrences (all)	0	1	13
CONFUSIONAL STATE			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 92 (1.09%)
occurrences (all)	0	1	1
DEPRESSION			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	11 / 92 (11.96%)
occurrences (all)	1	1	12
ENURESIS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	10 / 92 (10.87%)
occurrences (all)	0	1	12
TACHYPHRENIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	8 / 92 (8.70%)
occurrences (all)	2	0	13
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	6 / 92 (6.52%)
occurrences (all)	7	1	14
BLOOD ALBUMIN INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	1	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	5 / 92 (5.43%)
occurrences (all)	0	1	11
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 92 (2.17%)
occurrences (all)	1	0	3
BLOOD CREATINE INCREASED			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 92 (1.09%)
occurrences (all)	0	1	1
<b>BLOOD CREATININE INCREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	8 / 92 (8.70%)
occurrences (all)	0	1	38
<b>BLOOD MAGNESIUM DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	1	0
<b>BLOOD SODIUM DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	1	0
<b>GAMMA-GLUTAMYLTRANSFERASE DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	1	0
<b>GAMMA-GLUTAMYLTRANSFERASE INCREASED</b>			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	9 / 92 (9.78%)
occurrences (all)	1	3	41
<b>GRANULOCYTE COUNT DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	2	0
<b>HAEMOGLOBIN DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 92 (1.09%)
occurrences (all)	0	1	4
<b>PROTEIN TOTAL DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	1	0
<b>WEIGHT DECREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	6 / 92 (6.52%)
occurrences (all)	0	2	10
<b>WEIGHT INCREASED</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	5 / 92 (5.43%)
occurrences (all)	0	0	5
<b>Injury, poisoning and procedural complications</b>			

FALL subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	3 / 92 (3.26%) 4
Cardiac disorders BRADYCARDIA subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 92 (1.09%) 1
PALPITATIONS subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 92 (1.09%) 1
SINUS BRADYCARDIA subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	2 / 92 (2.17%) 2
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0	16 / 92 (17.39%) 25
DYSGEUSIA subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	13 / 92 (14.13%) 16
HEADACHE subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	20 / 92 (21.74%) 29
NEUROPATHY PERIPHERAL subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 3	0 / 3 (0.00%) 0	2 / 92 (2.17%) 2
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	1 / 3 (33.33%) 3	17 / 92 (18.48%) 48
INCREASED TENDENCY TO BRUISE subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	0 / 92 (0.00%) 0
LYMPHADENOPATHY subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 92 (1.09%) 1
NEUTROPENIA			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 6	1 / 3 (33.33%) 1	3 / 92 (3.26%) 6
THROMBOCYTOPENIA subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 3 (66.67%) 3	1 / 92 (1.09%) 2
Eye disorders DRY EYE subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	5 / 92 (5.43%) 6
PHOTOPSIA subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 92 (0.00%) 0
VISION BLURRED subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	5 / 92 (5.43%) 9
Gastrointestinal disorders ABDOMINAL PAIN subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	7 / 92 (7.61%) 8
ABDOMINAL PAIN UPPER subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	5 / 92 (5.43%) 6
CONSTIPATION subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	1 / 3 (33.33%) 1	21 / 92 (22.83%) 27
DIARRHOEA subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 3	0 / 3 (0.00%) 0	30 / 92 (32.61%) 50
DRY MOUTH subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	5 / 92 (5.43%) 7
DYSPEPSIA subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	6 / 92 (6.52%) 6
HAEMATOCHEZIA			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
<b>NAUSEA</b>			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	34 / 92 (36.96%)
occurrences (all)	1	3	53
<b>PROCTALGIA</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
<b>STOMATITIS</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 92 (6.52%)
occurrences (all)	0	0	11
<b>VOMITING</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	14 / 92 (15.22%)
occurrences (all)	0	0	20
<b>Skin and subcutaneous tissue disorders</b>			
<b>ALOPECIA</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	8 / 92 (8.70%)
occurrences (all)	0	0	10
<b>ECCHYMOSIS</b>			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences (all)	2	0	3
<b>NIGHT SWEATS</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 92 (3.26%)
occurrences (all)	1	0	3
<b>PRURITUS</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	13 / 92 (14.13%)
occurrences (all)	1	0	15
<b>RASH</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	11 / 92 (11.96%)
occurrences (all)	0	0	12
<b>SKIN MASS</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
<b>Renal and urinary disorders</b>			
<b>BLADDER SPASM</b>			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
<b>DYSURIA</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 92 (1.09%)
occurrences (all)	1	0	1
<b>POLLAKIURIA</b>			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 92 (2.17%)
occurrences (all)	0	0	2
<b>URINARY HESITATION</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 92 (0.00%)
occurrences (all)	1	0	0
<b>Musculoskeletal and connective tissue disorders</b>			
<b>ARTHRALGIA</b>			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	28 / 92 (30.43%)
occurrences (all)	2	1	60
<b>BACK PAIN</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	29 / 92 (31.52%)
occurrences (all)	0	1	49
<b>BONE LOSS</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 92 (0.00%)
occurrences (all)	0	1	0
<b>BONE PAIN</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	9 / 92 (9.78%)
occurrences (all)	3	0	9
<b>FLANK PAIN</b>			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 92 (2.17%)
occurrences (all)	1	0	2
<b>GROIN PAIN</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	2 / 92 (2.17%)
occurrences (all)	0	1	2
<b>MUSCLE SPASMS</b>			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	10 / 92 (10.87%)
occurrences (all)	0	2	12
<b>MUSCULOSKELETAL CHEST PAIN</b>			

subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	1 / 3 (33.33%) 1	12 / 92 (13.04%) 15
<b>MUSCULOSKELETAL PAIN</b> subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0	10 / 92 (10.87%) 13
<b>MYALGIA</b> subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 5	1 / 3 (33.33%) 1	9 / 92 (9.78%) 10
<b>NECK PAIN</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	6 / 92 (6.52%) 7
<b>PAIN IN EXTREMITY</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	14 / 92 (15.22%) 20
<b>Infections and infestations</b>			
<b>BRONCHITIS</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	2 / 92 (2.17%) 2
<b>DEVICE RELATED INFECTION</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 92 (0.00%) 0
<b>FUNGAL SKIN INFECTION</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 92 (0.00%) 0
<b>INFLUENZA</b> subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	2 / 92 (2.17%) 2
<b>LIP INFECTION</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 3	0 / 92 (0.00%) 0
<b>NAIL INFECTION</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	1 / 92 (1.09%) 1
<b>SINUSITIS</b> subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	4 / 92 (4.35%) 4

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	9 / 92 (9.78%)
occurrences (all)	0	0	11
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	26 / 92 (28.26%)
occurrences (all)	1	1	48
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	6 / 92 (6.52%)
occurrences (all)	0	0	7
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	19 / 92 (20.65%)
occurrences (all)	1	0	24
DEHYDRATION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 92 (1.09%)
occurrences (all)	0	1	2
DIABETES MELLITUS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	3 / 92 (3.26%)
occurrences (all)	1	0	5
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	10 / 92 (10.87%)
occurrences (all)	0	5	38
HYPERKALAEMIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	5 / 92 (5.43%)
occurrences (all)	1	0	5
HYPERMAGNESAEMIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 92 (2.17%)
occurrences (all)	1	0	2
HYPERURICAEMIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	5 / 92 (5.43%)
occurrences (all)	1	0	6
HYPOCALCAEMIA			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	7 / 92 (7.61%)
occurrences (all)	3	0	15
HYPOKALAEMIA			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	10 / 92 (10.87%) 18
<b>HYPOMAGNESAEMIA</b> subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1	6 / 92 (6.52%) 9
<b>HYPONATRAEMIA</b> subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 5	0 / 3 (0.00%) 0	3 / 92 (3.26%) 16
<b>HYPOPHOSPATAEMIA</b> subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 3	0 / 3 (0.00%) 0	2 / 92 (2.17%) 2

<b>Non-serious adverse events</b>	Aromatase Inhibitor		
Total subjects affected by non-serious adverse events subjects affected / exposed	82 / 85 (96.47%)		
<b>Vascular disorders</b>			
<b>HOT FLUSH</b> subjects affected / exposed occurrences (all)	30 / 85 (35.29%) 46		
<b>HYPERTENSION</b> subjects affected / exposed occurrences (all)	13 / 85 (15.29%) 24		
<b>PERIPHERAL COLDNESS</b> subjects affected / exposed occurrences (all)	0 / 85 (0.00%) 0		
<b>General disorders and administration site conditions</b>			
<b>ASTHENIA</b> subjects affected / exposed occurrences (all)	13 / 85 (15.29%) 18		
<b>FATIGUE</b> subjects affected / exposed occurrences (all)	27 / 85 (31.76%) 38		
<b>MUCOSAL INFLAMMATION</b> subjects affected / exposed occurrences (all)	0 / 85 (0.00%) 0		
<b>OEDEMA PERIPHERAL</b>			

<p>subjects affected / exposed occurrences (all)</p> <p>PAIN</p> <p>subjects affected / exposed occurrences (all)</p> <p>PYREXIA</p> <p>subjects affected / exposed occurrences (all)</p> <p>SWELLING</p> <p>subjects affected / exposed occurrences (all)</p>	<p>10 / 85 (11.76%) 20</p> <p>1 / 85 (1.18%) 1</p> <p>6 / 85 (7.06%) 11</p> <p>1 / 85 (1.18%) 1</p>		
<p>Reproductive system and breast disorders</p> <p>ATROPHIC VULVOVAGINITIS</p> <p>subjects affected / exposed occurrences (all)</p> <p>BREAST HAEMORRHAGE</p> <p>subjects affected / exposed occurrences (all)</p> <p>BREAST PAIN</p> <p>subjects affected / exposed occurrences (all)</p>	<p>1 / 85 (1.18%) 1</p> <p>0 / 85 (0.00%) 0</p> <p>5 / 85 (5.88%) 9</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>COUGH</p> <p>subjects affected / exposed occurrences (all)</p> <p>DYSPNOEA</p> <p>subjects affected / exposed occurrences (all)</p> <p>DYSPNOEA EXERTIONAL</p> <p>subjects affected / exposed occurrences (all)</p> <p>EPISTAXIS</p> <p>subjects affected / exposed occurrences (all)</p> <p>OROPHARYNGEAL PAIN</p>	<p>11 / 85 (12.94%) 16</p> <p>14 / 85 (16.47%) 23</p> <p>2 / 85 (2.35%) 2</p> <p>2 / 85 (2.35%) 5</p>		

subjects affected / exposed occurrences (all)	4 / 85 (4.71%) 4		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	8 / 85 (9.41%)		
occurrences (all)	10		
CONFUSIONAL STATE			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
DEPRESSION			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	4		
ENURESIS			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
INSOMNIA			
subjects affected / exposed	13 / 85 (15.29%)		
occurrences (all)	14		
TACHYPHRENIA			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	5		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	7		
BLOOD ALBUMIN INCREASED			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	5 / 85 (5.88%)		
occurrences (all)	10		
BLOOD CHOLESTEROL INCREASED			

subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	3		
<b>BLOOD CREATINE INCREASED</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>BLOOD CREATININE INCREASED</b>			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	2		
<b>BLOOD MAGNESIUM DECREASED</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>BLOOD SODIUM DECREASED</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>GAMMA-GLUTAMYLTRANSFERASE DECREASED</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>GAMMA-GLUTAMYLTRANSFERASE INCREASED</b>			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	5		
<b>GRANULOCYTE COUNT DECREASED</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>HAEMOGLOBIN DECREASED</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>PROTEIN TOTAL DECREASED</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	2		
<b>WEIGHT DECREASED</b>			
subjects affected / exposed	5 / 85 (5.88%)		
occurrences (all)	7		
<b>WEIGHT INCREASED</b>			

subjects affected / exposed occurrences (all)	3 / 85 (3.53%) 3		
Injury, poisoning and procedural complications FALL subjects affected / exposed occurrences (all)	6 / 85 (7.06%) 6		
Cardiac disorders BRADYCARDIA subjects affected / exposed occurrences (all)  PALPITATIONS subjects affected / exposed occurrences (all)  SINUS BRADYCARDIA subjects affected / exposed occurrences (all)	1 / 85 (1.18%) 1  2 / 85 (2.35%) 3  0 / 85 (0.00%) 0		
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all)  DYSGEUSIA subjects affected / exposed occurrences (all)  HEADACHE subjects affected / exposed occurrences (all)  NEUROPATHY PERIPHERAL subjects affected / exposed occurrences (all)	9 / 85 (10.59%) 12  8 / 85 (9.41%) 8  19 / 85 (22.35%) 27  2 / 85 (2.35%) 3		
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all)  INCREASED TENDENCY TO BRUISE subjects affected / exposed occurrences (all)	10 / 85 (11.76%) 18  1 / 85 (1.18%) 1		

<p>LYMPHADENOPATHY</p> <p>subjects affected / exposed</p> <p>1 / 85 (1.18%)</p> <p>occurrences (all)</p> <p>1</p>			
<p>NEUTROPENIA</p> <p>subjects affected / exposed</p> <p>4 / 85 (4.71%)</p> <p>occurrences (all)</p> <p>8</p>			
<p>THROMBOCYTOPENIA</p> <p>subjects affected / exposed</p> <p>3 / 85 (3.53%)</p> <p>occurrences (all)</p> <p>11</p>			
<p>Eye disorders</p> <p>DRY EYE</p> <p>subjects affected / exposed</p> <p>6 / 85 (7.06%)</p> <p>occurrences (all)</p> <p>7</p> <p>PHOTOPSIA</p> <p>subjects affected / exposed</p> <p>0 / 85 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>VISION BLURRED</p> <p>subjects affected / exposed</p> <p>2 / 85 (2.35%)</p> <p>occurrences (all)</p> <p>2</p>			
<p>Gastrointestinal disorders</p> <p>ABDOMINAL PAIN</p> <p>subjects affected / exposed</p> <p>7 / 85 (8.24%)</p> <p>occurrences (all)</p> <p>9</p> <p>ABDOMINAL PAIN UPPER</p> <p>subjects affected / exposed</p> <p>6 / 85 (7.06%)</p> <p>occurrences (all)</p> <p>9</p> <p>CONSTIPATION</p> <p>subjects affected / exposed</p> <p>23 / 85 (27.06%)</p> <p>occurrences (all)</p> <p>32</p> <p>DIARRHOEA</p> <p>subjects affected / exposed</p> <p>22 / 85 (25.88%)</p> <p>occurrences (all)</p> <p>39</p> <p>DRY MOUTH</p> <p>subjects affected / exposed</p> <p>8 / 85 (9.41%)</p> <p>occurrences (all)</p> <p>13</p> <p>DYSPEPSIA</p>			

subjects affected / exposed	6 / 85 (7.06%)		
occurrences (all)	8		
<b>HAEMATOCHEZIA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>NAUSEA</b>			
subjects affected / exposed	30 / 85 (35.29%)		
occurrences (all)	46		
<b>PROCTALGIA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>STOMATITIS</b>			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	9		
<b>VOMITING</b>			
subjects affected / exposed	15 / 85 (17.65%)		
occurrences (all)	21		
<b>Skin and subcutaneous tissue disorders</b>			
<b>ALOPECIA</b>			
subjects affected / exposed	11 / 85 (12.94%)		
occurrences (all)	12		
<b>ECCHYMOSIS</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>NIGHT SWEATS</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>PRURITUS</b>			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences (all)	9		
<b>RASH</b>			
subjects affected / exposed	10 / 85 (11.76%)		
occurrences (all)	15		
<b>SKIN MASS</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		

Renal and urinary disorders			
BLADDER SPASM			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
DYSURIA			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	1		
POLLAKIURIA			
subjects affected / exposed	6 / 85 (7.06%)		
occurrences (all)	7		
URINARY HESITATION			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	35 / 85 (41.18%)		
occurrences (all)	73		
BACK PAIN			
subjects affected / exposed	21 / 85 (24.71%)		
occurrences (all)	33		
BONE LOSS			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
BONE PAIN			
subjects affected / exposed	9 / 85 (10.59%)		
occurrences (all)	11		
FLANK PAIN			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	1		
GROIN PAIN			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	1		
MUSCLE SPASMS			
subjects affected / exposed	8 / 85 (9.41%)		
occurrences (all)	14		
MUSCULOSKELETAL CHEST PAIN			

subjects affected / exposed	11 / 85 (12.94%)		
occurrences (all)	14		
<b>MUSCULOSKELETAL PAIN</b>			
subjects affected / exposed	11 / 85 (12.94%)		
occurrences (all)	12		
<b>MYALGIA</b>			
subjects affected / exposed	10 / 85 (11.76%)		
occurrences (all)	11		
<b>NECK PAIN</b>			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences (all)	8		
<b>PAIN IN EXTREMITY</b>			
subjects affected / exposed	18 / 85 (21.18%)		
occurrences (all)	43		
<b>Infections and infestations</b>			
<b>BRONCHITIS</b>			
subjects affected / exposed	6 / 85 (7.06%)		
occurrences (all)	7		
<b>DEVICE RELATED INFECTION</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>FUNGAL SKIN INFECTION</b>			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	3		
<b>INFLUENZA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>LIP INFECTION</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>NAIL INFECTION</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
<b>SINUSITIS</b>			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences (all)	4		

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 85 (11.76%)		
occurrences (all)	13		
URINARY TRACT INFECTION			
subjects affected / exposed	17 / 85 (20.00%)		
occurrences (all)	26		
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	7 / 85 (8.24%)		
occurrences (all)	7		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	14 / 85 (16.47%)		
occurrences (all)	16		
DEHYDRATION			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	2		
DIABETES MELLITUS			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		
HYPERGLYCAEMIA			
subjects affected / exposed	8 / 85 (9.41%)		
occurrences (all)	12		
HYPERKALAEMIA			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences (all)	13		
HYPERMAGNESAEMIA			
subjects affected / exposed	3 / 85 (3.53%)		
occurrences (all)	6		
HYPERURICAEMIA			
subjects affected / exposed	2 / 85 (2.35%)		
occurrences (all)	3		
HYPOCALCAEMIA			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	1		
HYPOKALAEMIA			

subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	12		
<b>HYPOMAGNESAEMIA</b>			
subjects affected / exposed	1 / 85 (1.18%)		
occurrences (all)	2		
<b>HYPONATRAEMIA</b>			
subjects affected / exposed	4 / 85 (4.71%)		
occurrences (all)	7		
<b>HYPOPHOSPATAEMIA</b>			
subjects affected / exposed	0 / 85 (0.00%)		
occurrences (all)	0		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 February 2012	Sections of clinical experience with medi-573, research hypothesis, research hypothesis were updated. Primary objective was updated for the number of dose levels to be tested from 2 to 3. The text of Phase 1b (Dose-evaluation Phase) was modified to account for the addition of a 45 mg/kg plus AI treatment arm. Phase 2 (Randomization Phase) was changed to a 2-arm structure to test 45 mg/kg MEDI-573 plus AI versus AI alone. Addition of a 45 mg/kg arm in Phase 1b and Phase 2, based on PK and pharmacodynamic experience. Inclusion criteria added for participants with metastases to bone, clarified that HER2 negativity assessment, added the definition of postmenopausal, and added the age limit for participants enrolled in Japan. Exclusion criteria changed for the washout period following tamoxifen or an AI prior to receiving the first dose of MEDI-573, clarified the exclusion of participants with active brain metastases, known central nervous system metastases, and leptomeningeal carcinomatosis; text was modified for participants with a history of allergy or reaction attributed to compounds of chemical/biologic composition similar to MEDI-573 or AI, for history of another invasive malignancy, and had poorly controlled diabetes mellitus. Modified the randomization text. Added the text related to dairy for AI intake. Clarified the for MEDI-573 infusion timing. Updated the "Schedule of Study Procedures" table. Added additional physical examination details. Planned analyses text was changed to specify that the primary analysis of PFS and safety were performed after 122 PFS events had occurred. Modified sample size and power calculations.
05 December 2012	Randomization statement was added for participants with bone-only disease. Inclusion criteria were updated for participants with bone metastases and method of determining HER2 status. Exclusion criteria were updated for prior adjuvant therapy with an AI and/or tamoxifen and participants with evidence of spinal canal involvement. Added treatment window period to infusion times for potential overfill and for collection of vital signs. Updated permitted concomitant medications section. Updated the "Schedule of Study Procedures" table. Screening section was modified for laboratory results, pregnancy tests, and archival tumor samples. Modified the statements related to Cycle 1 Day 1 and Cycle 2 and Every Cycle Thereafter assessments. Added the description of assessments required after 2 years on study for participants who remain on study drug or s who were discontinued study drug.
25 July 2016	Updated the text to include the results from the completed FTIH study (CP-184) and the primary analysis of CD-ON-MEDI-573-1030 study. Updated "End of study" to clarify the follow-up procedures for participants who discontinued treatment or for participants who were on treatment at the end of 36 months. Updated the "Schedule of Study Procedures" table.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported