Clinical trial results:
Phase IB/II clinical trial of copanlisib in combination with trastuzumab in pretreated recurrent or metastatic HER2-positive breast cancer

Summary

EudraCT number	2015-003687-36
Trial protocol	IE
Global end of trial date	06 May 2022

Results information

Result version number	v1 (current)
This version publication date	25 April 2026
First version publication date	25 April 2026

Trial information

Trial identification

Sponsor protocol code	CTRIAL 15-02 (ICORG)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02705859
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cancer Trials Ireland CLG
Sponsor organisation address	RCSI House, Dublin 01, Ireland,
Public contact	Ausra Teiserskiene, Cancer Trials Ireland CLG, +353 16677211, info@cancertrials.ie
Scientific contact	Prof Bryan Hennessy, Cancer Trials Ireland CLG, +353 16677211, info@cancertrials.ie

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	09 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase Ib
1. To determine the Maximum Tolerated Dose (MTD), for copanlisib in combination with trastuzumab in patients with histologically confirmed HER2-positive breast cancer that are metastatic or incurable recurrent, following disease progression during, or after, treatment with at least one systemic treatment regimen in the metastatic or recurrent setting.

Phase II
1. To evaluate the anti-tumour efficacy of copanlisib in combination with trastuzumab in terms of Clinical Benefit Rate (CBR) in patients with PIK3CA wild type and mutated, histologically confirmed HER2-positive breast cancer that are metastatic or incurable recurrent, following disease progression during, or after, treatment with at least one systemic treatment regimen in the metastatic or recurrent setting (Phase II plus patients with PIK3CA wild type and mutated HER2-positive breast cancer treated at MTD in Phase Ib).

Protection of trial subjects:

Timely, accurate and complete reporting and analysis of safety information from clinical studies are crucial for the protection of patients and are mandated by regulatory agencies worldwide.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	24
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants will be patients of the study doctor and his/her medical team and approached about the study in clinic.

Pre-assignment

Screening details:

Potential patients will be screened and enrolled on the study on the basis of the Inclusion/Exclusion criteria specified in the protocol. Before registration, each potential patient must be given a patient information leaflet (PIL) and informed consent must be obtained from a patient according to the requirements of ICH GCP.

Period 1

Period 1 title	Phase Ib/II
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Copanlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

IV weekly for the first 3 weeks (on days 1, 8, 15) of a 28-day cycle 45 mg flat dosing

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Trastuzumab IV weekly (4 mg/kg on Cycle 1 Day 1 followed by 2 mg/kg IV weekly from Day 8).

Arm title	Arm 2

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Copanlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

IV weekly for the first 3 weeks (on days 1, 8, 15) of a 28-day cycle 60 mg flat dosing

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Trastuzumab IV weekly (4 mg/kg on Cycle 1 Day 1 followed by 2 mg/kg IV weekly from Day 8).

Number of subjects in period 1	Arm 1	Arm 2
Started	6	20
Completed	6	20

Period 2

Period 2 title	Full Analysis Set
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Arm 2

Arm description:

The Full Analysis Set includes the 6 patients from Phase Ib treated at the MTD, and 13 of 14 enrolled patients from Phase II. The one Phase II patient excluded from the FAS had a toxicity reaction of hyperglycemia related to copanlisib treatment during Cycle 1. This patient was withdrawn from the study prior to post-baseline disease response assessment.

Arm type	Experimental
Investigational medicinal product name	Copanlisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

IV weekly for the first 3 weeks (on days 1, 8, 15) of a 28-day cycle 60 mg flat dosing

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Trastuzumab IV weekly (4 mg/kg on Cycle 1 Day 1 followed by 2 mg/kg IV weekly from Day 8).

Number of subjects in period 2[1]	Arm 2
Started	19
Completed	19

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The efficacy analyses were performed on the Full Analysis Set (FAS), which is defined as all patients who were given a starting copanlisib dose of 60 mg and either had at least one post-baseline response assessment or exhibited disease progression or died prior to their first scheduled post-baseline radiologic tumor response assessment.

The Full Analysis Set includes the 6 patients from Phase Ib treated at the MTD, and 13 of 14 enrolled patients from Phase II. The one Phase II patient excluded

Baseline characteristics

Reporting groups	
Reporting group title	Phase Ib/II

Reporting group description: -

Reporting group values	Phase Ib/II	Total	
Number of subjects	26	26	
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)	24	24	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	52.23		
full range (min-max)	40 to 79	-	
Gender categorical Units: Subjects			
Female	26	26	
Male	0	0	
Ethnic Group Units: Subjects			
Hispanic or Latino		0	
Not Hispanic or Latino	25	25	
Not Reported	1	1	
Primary Tumor Location Units: Subjects			
Breast	26	26	
Primary Tumor Laterality Units: Subjects			
Left	16	16	
Right	10	10	
Height at Screening Units: centimetre			
arithmetic mean	165.4		
full range (min-max)	153.1 to 181	-	
Weight at Screening Units: kilogram(s)			
arithmetic mean	73.9		
full range (min-max)	43.1 to 106.3	-	

Duration of Initial Diagnosis to Registration			
Units: day			
arithmetic mean	2225.04		
full range (min-max)	315 to 5200	-	
Duration from Most Recent Progression to Registration			
Units: day			
arithmetic mean	84.85		
full range (min-max)	7 to 996	-	
Duration from First Recurrence to Registration			
Units: day			
arithmetic mean	1314.5		
full range (min-max)	312 to 4197	-	

Subject analysis sets	
Subject analysis set title	Phase IB/II 60 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
This subject analysis set includes all patients who received at least one dose of copanlisib 60 mg.	
Subject analysis set title	Phase IB 45mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
This subject analysis set includes all patients who received at least one dose of copanlisib 45 mg.	

Reporting group values	Phase IB/II 60 mg	Phase IB 45mg	
Number of subjects	20	6	
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)	24	5	
From 65-84 years	2	1	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	51.2	53	
full range (min-max)	40 to 79	50 to 72	
Gender categorical			
Units: Subjects			
Female	20	6	
Male	0	0	
Ethnic Group			
Units: Subjects			
Hispanic or Latino	0		

Not Hispanic or Latino	19	6	
Not Reported	1		
Primary Tumor Location Units: Subjects			
Breast	20	6	
Primary Tumor Laterality Units: Subjects			
Left	12	4	
Right	8	2	
Height at Screening Units: centimetre			
arithmetic mean	165.55	164.92	
full range (min-max)	153.1 to 181.0	159 to 178	
Weight at Screening Units: kilogram(s)			
arithmetic mean	70.92	83.83	
full range (min-max)	43.1 to 101.1	57.1 to 106.3	
Duration of Initial Diagnosis to Registration Units: day			
arithmetic mean	2153.5	2463.5	
full range (min-max)	315 to 3571	593 to 5200	
Duration from Most Recent Progression to Registration Units: day			
arithmetic mean	93.9	54.7	
full range (min-max)	7 to 996	29 to 105	
Duration from First Recurrence to Registration Units: day			
arithmetic mean	1195.4	1711.5	
full range (min-max)	312 to 2757	574 to 4197	

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description: -	
Reporting group title	Arm 2
Reporting group description: -	
Reporting group title	Arm 2

Reporting group description:

The Full Analysis Set includes the 6 patients from Phase Ib treated at the MTD, and 13 of 14 enrolled patients from Phase II. The one Phase II patient excluded from the FAS had a toxicity reaction of hyperglycemia related to copanlisib treatment during Cycle 1. This patient was withdrawn from the study prior to post-baseline disease response assessment.

Subject analysis set title	Phase IB/II 60 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

This subject analysis set includes all patients who received at least one dose of copanlisib 60 mg.

Subject analysis set title	Phase IB 45mg
Subject analysis set type	Safety analysis

Subject analysis set description:

This subject analysis set includes all patients who received at least one dose of copanlisib 45 mg.

Primary: Summary of Clinical Benefit

End point title	Summary of Clinical Benefit[1]

End point description:

The primary endpoint of Phase II was the anti-tumor efficacy analysis in terms of CBR. A target CBR of 65% was set based on the efficacy of existing treatments. Analysis of the CBR was performed on the FAS, which is defined as all patients who were given a starting copanlisib dose of 60 mg and either had at least one post-baseline response assessment or exhibited disease progression or died prior to their first scheduled post-baseline radiologic tumor response assessment.

End point type	Primary

End point timeframe:

CBR for this study was defined as CR or PR at any time during the study or SD lasting at least 24 weeks. In the analysis, SD lasting at least 24 weeks was defined as 168 or more between registration and the patient’s first reported disease progression

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: The CBR of 36.8% shown in this trial of copanlisib plus trastuzumab is marginally better than the 30% that was considered the lowest acceptable CBR for this trial due to a 34% CBR having been shown in Phase II-III trials for fellow PI3K inhibitor RAD001 plus trastuzumab in a similar population. The CBR of 36.8%, however, does not approach the conservative goal set for this trial of 65%. Since the two-sided 90% CI of (21.4%, 55.6%) around the CBR contains the null hypothesis of 30%, the statistic

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Subject				
Clinical Benefit Rate	7			
CR at any timepoint	0			
PR at any timepoint	4			
SD lasting at least 24 weeks	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

overall survival time, which is defined as the time from registration to death from any cause.

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Subjects				
Number of Patients with Event	12			
Number of Patients Censored	7			
Median Time to Event (days)	450			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival Rate (95% CI)

End point title	Overall Survival Rate (95% CI)

End point description:

End point type	Secondary

End point timeframe:

overall survival time, which is defined as the time from registration to death from any cause.

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: days				
median (full range (min-max))				
1 Year (365 Days)	56.1 (31.1 to 75.2)			
2 Years (730 Days)	37.4 (15.6 to 59.4)			
3 Years (1095 Days)	28.1 (8.5 to 52)			
4 Years (1461 Days)	28.1 (8.5 to 52)			
End of Study (1675 Days)	28.1 (8.5 to 52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

To be consistent with the definition of stable disease lasting at least 24 weeks in the CBR analysis, termination of treatment or study follow-up reportedly due to progression is considered to be a progression event for the PFS analysis, even in the absence of a corresponding confirmatory radiologic assessment. In the absence of progression or death, patients were censored at the date of their last radiologic tumor assessment

End point type	Secondary

End point timeframe:

PFS is defined as the time from study registration to disease progression or death from any cause

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Subjects				
Number of Patients with Event	18			
Number of Patients Censored	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival Rate (95% CI)

End point title	Progression Free Survival Rate (95% CI)

End point description:

End point type	Secondary

End point timeframe:

PFS is defined as the time from study registration to disease progression or death from any cause

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: days				
median (full range (min-max))				
Median Time to Event (days) (95% CI) 6 Months (182 Days) End of Study (295 Days)	113.0 (57.0 to 168.0) 22.6 (7.0 to 43.4) 0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure

End point title	Time to Treatment Failure

End point description:

To be consistent with the PFS analysis, termination of treatment or study follow-up reportedly due to progression is considered to be a treatment failure event for the TTF analysis, even in the absence of a corresponding confirmatory radiologic assessment. In the absence of a treatment failure event, patients were censored at the date of their last radiologic tumor assessment.

End point type	Secondary

End point timeframe:

Time from registration to the discontinuation of therapy for any reason (including death, progression, and toxicity) or add-on of any new anti-cancer therapy

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Subjects				
Number of Patients with Event Number of Patients Censored	19 0			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure Rate (95% CI)

End point title	Time to Treatment Failure Rate (95% CI)

End point description:

End point type	Secondary

End point timeframe:

Time from registration to the discontinuation of therapy for any reason (including death, progression, and toxicity), or add-on of any new anti cancer therapy

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: days				
median (full range (min-max))				
Median Time to Event (days) (95% CI) 6 Months (182 Days)	113.0 (51.0 to 168.0) 78.9 (59.0 to 93.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Of the 4 patients who achieved a partial response, the response duration ranged from 35 days to 115 days, with a median of 106 days.

End point type	Secondary

End point timeframe:

Duration of response is calculated as the number of days from the first CR or PR to disease progression or death.

End point values	Arm 2			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: days				
median (full range (min-max))				
Median	106.0 (35 to 115)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Emergent Adverse Events, those that occur same date or after administration of the first study dose.

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Phase IB/II - 60 mg Copanlisib

Reporting group description: -

Reporting group title	Phase IB - 45 mg Copanlisib

Reporting group description: -

Serious adverse events	Phase IB/II - 60 mg Copanlisib	Phase IB - 45 mg Copanlisib	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 20 (40.00%)	5 / 6 (83.33%)	
number of deaths (all causes)	12	5	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphangiosis carcinomatosa	Additional description: Lymphangiosis carcinomatosa		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction	Additional description: Infusion related reaction		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture	Additional description: Hip fracture		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Headache	Additional description: Headache		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure	Additional description: Seizure		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pain	Additional description: Pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Photophobia	Additional description: Photophobia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction	Additional description: Biliary obstruction		

subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection	Additional description: Infection		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 20 (0.00%)	2 / 6 (33.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Phase IB/II - 60 mg Copanlisib	Phase IB - 45 mg Copanlisib	
Total subjects affected by non-serious adverse events subjects affected / exposed	20 / 20 (100.00%)	6 / 6 (100.00%)	
Vascular disorders			
Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Hypertension	Additional description: Hypertension		
subjects affected / exposed	5 / 20 (25.00%)	5 / 6 (83.33%)	
occurrences (all)	22	35	
White coat hypertension	Additional description: White coat hypertension		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Nail operation	Additional description: Nail operation		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Axillary pain	Additional description: Axillary pain		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	8 / 20 (40.00%)	4 / 6 (66.67%)	
occurrences (all)	15	9	
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infusion site extravasation	Additional description: Infusion site extravasation		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infusion site pain	Additional description: Infusion site pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

Medical device site pain	Additional description: Medical device site pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	4 / 20 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	7	4	
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Pain	Additional description: Pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling	Additional description: Peripheral swelling		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	5	0	
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	3 / 20 (15.00%)	3 / 6 (50.00%)	
occurrences (all)	4	6	
Reproductive system and breast disorders			
Breast pain	Additional description: Breast pain		
subjects affected / exposed	3 / 20 (15.00%)	3 / 6 (50.00%)	
occurrences (all)	3	3	
Respiratory, thoracic and mediastinal disorders			
Dysphonia	Additional description: Dysphonia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	3 / 20 (15.00%)	1 / 6 (16.67%)	
occurrences (all)	6	2	
Cough	Additional description: Cough		
subjects affected / exposed	3 / 20 (15.00%)	3 / 6 (50.00%)	
occurrences (all)	5	3	
Laryngeal inflammation	Additional description: Laryngeal inflammation		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nasal congestion	Additional description: Nasal congestion		

subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nasal discomfort	Additional description: Nasal discomfort		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Productive cough	Additional description: Productive cough		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	2	
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory symptom	Additional description: Respiratory symptom		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea	Additional description: Rhinorrhoea		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Wheezing	Additional description: Wheezing		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety	Additional description: Anxiety		
subjects affected / exposed	3 / 20 (15.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Agitation	Additional description: Agitation		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Confusional state	Additional description: Confusional state		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Insomnia	Additional description: Insomnia		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	

Investigations			
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Blood pressure increased	Additional description: Blood pressure increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Haemoglobin decreased	Additional description: Haemoglobin decreased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Weight decreased	Additional description: Weight decreased		

subjects affected / exposed	2 / 20 (10.00%)	3 / 6 (50.00%)	
occurrences (all)	2	4	
Troponin increased	Additional description: Troponin increased		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall	Additional description: Fall		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Tooth fracture	Additional description: Tooth fracture		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	4 / 20 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	7	6	
Migraine	Additional description: Migraine		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	2 / 20 (10.00%)	1 / 6 (16.67%)	
occurrences (all)	12	2	
Paralysis recurrent laryngeal nerve	Additional description: Paralysis recurrent laryngeal nerve		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Peripheral motor neuropathy	Additional description: Peripheral motor neuropathy		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Spinal cord compression	Additional description: Spinal cord compression		

subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	4 / 20 (20.00%)	1 / 6 (16.67%)	
occurrences (all)	8	1	
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Eye disorders			
Dry eye	Additional description: Dry eye		
subjects affected / exposed	2 / 20 (10.00%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 20 (10.00%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	8 / 20 (40.00%)	3 / 6 (50.00%)	
occurrences (all)	35	8	
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	3 / 20 (15.00%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Constipation	Additional description: Constipation		
subjects affected / exposed	6 / 20 (30.00%)	3 / 6 (50.00%)	
occurrences (all)	15	5	
Colitis	Additional description: Colitis		

subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Chapped lips	Additional description: Chapped lips		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Lip pain	Additional description: Lip pain		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nausea	Additional description: Nausea		
subjects affected / exposed	11 / 20 (55.00%)	3 / 6 (50.00%)	
occurrences (all)	23	21	
Oral mucosal blistering	Additional description: Oral mucosal blistering		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Oral disorder	Additional description: Oral disorder		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Paraesthesia oral	Additional description: Paraesthesia oral		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed	8 / 20 (40.00%)	4 / 6 (66.67%)	
occurrences (all)	13	7	
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	5 / 20 (25.00%)	3 / 6 (50.00%)	
occurrences (all)	14	8	
Skin and subcutaneous tissue disorders			
Blood blister	Additional description: Blood blister		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

Dry skin	Additional description: Dry skin		
subjects affected / exposed	3 / 20 (15.00%)	3 / 6 (50.00%)	
occurrences (all)	4	5	
Dermatitis acneiform	Additional description: Dermatitis acneiform		
subjects affected / exposed	2 / 20 (10.00%)	2 / 6 (33.33%)	
occurrences (all)	4	3	
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pruritus	Additional description: Pruritus		
subjects affected / exposed	3 / 20 (15.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Rash	Additional description: Rash		
subjects affected / exposed	7 / 20 (35.00%)	2 / 6 (33.33%)	
occurrences (all)	9	3	
Rash erythematous	Additional description: Rash erythematous		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Rash pruritic	Additional description: Rash pruritic		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Scar pain	Additional description: Scar pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Skin lesion	Additional description: Skin lesion		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	1 / 20 (5.00%)	2 / 6 (33.33%)	
occurrences (all)	3	5	
Renal and urinary disorders			
Dysuria	Additional description: Dysuria		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Haematuria	Additional description: Haematuria		

subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nocturia	Additional description: Nocturia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Proteinuria	Additional description: Proteinuria		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 20 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Back pain	Additional description: Back pain		
subjects affected / exposed	2 / 20 (10.00%)	2 / 6 (33.33%)	
occurrences (all)	3	3	
Flank pain	Additional description: Flank pain		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	1 / 20 (5.00%)	2 / 6 (33.33%)	
occurrences (all)	1	2	
Myalgia	Additional description: Myalgia		
subjects affected / exposed	3 / 20 (15.00%)	0 / 6 (0.00%)	
occurrences (all)	8	0	
Neck pain	Additional description: Neck pain		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Pain in extremity	Additional description: Pain in extremity		

subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Infections and infestations			
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Herpes simplex	Additional description: Herpes simplex		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infection	Additional description: Infection		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Localised infection	Additional description: Localised infection		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	3	
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	2 / 20 (10.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Mastitis	Additional description: Mastitis		
subjects affected / exposed	0 / 20 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	4	
Mucosal infection	Additional description: Mucosal infection		
subjects affected / exposed	0 / 20 (0.00%)	2 / 6 (33.33%)	
occurrences (all)	0	2	
Nail infection	Additional description: Nail infection		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	2 / 20 (10.00%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	

Paronychia	Additional description: Paronychia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 20 (0.00%)	3 / 6 (50.00%)	
occurrences (all)	0	5	
Skin infection	Additional description: Skin infection		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	2 / 20 (10.00%)	2 / 6 (33.33%)	
occurrences (all)	2	4	
Vulvovaginal candidiasis	Additional description: Vulvovaginal candidiasis		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Dehydration	Additional description: Dehydration		
subjects affected / exposed	1 / 20 (5.00%)	2 / 6 (33.33%)	
occurrences (all)	2	2	
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	4 / 20 (20.00%)	3 / 6 (50.00%)	
occurrences (all)	5	3	
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	4 / 20 (20.00%)	4 / 6 (66.67%)	
occurrences (all)	7	24	
Hypertriglyceridaemia	Additional description: Hypertriglyceridaemia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		

subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	1 / 20 (5.00%)	1 / 6 (16.67%)	
occurrences (all)	2	2	
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	2 / 20 (10.00%)	2 / 6 (33.33%)	
occurrences (all)	2	3	
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 20 (5.00%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Iron deficiency	Additional description: Iron deficiency		
subjects affected / exposed	0 / 20 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2016	ICORG 15-02 Panther study Protocol Version 4 01February 2016 BAY 80-6946 (Copanlisib) Investigator's Brochure Amendment, Version 7.0 dated 23APR2015 CORRECTED Global Amendment 2.0 22DEC2015 Updated reconstruction instructions for the vials with the new fill volume as outlined in the corrected IB addendum
27 June 2016	ICORG 15-02 PantHER Study Protocol Version 5 05 May 2016 ICORG Phase I Committee Charter Version 1/05-May-2016
13 February 2017	Updates to several sections of the protocol to Protocol v6.0 (13Jan2017). The Investigator’s Brochure (IB) was amended in response to questions received from the United Kingdom and Belgian Health Authorities.
21 March 2018	The protocol was amended to Protocol v7 (24Jan2018) in line with the recent completion of study Phase Ib and planned commencement of study Phase II. Updates have occurred to several sections of the protocol. The Investigator’s Brochure (IB) v10.0 10 AUG 2017 Amendment Number: 1.0 04 JAN 2018 was amended in response to a request from a Health Authority regarding the expectedness table in Reference Safety Information (RSI) and following the recently published European Union (EU) Clinical Trial Facilitation Group (CTFG) guidance on RSI (published in NOV 2017). The expectedness Table 8–1 in the RSI section has been revised based on Serious Adverse Reactions (SARs) considered expected for safety reporting purposes. No new SARs have been added as compared to the RSI in IB v10.0. Additionally, the previous Table 8–1 reflecting the overall safety profile of copanlisib has been moved to Section 9.6 Undesirable Effects in the Core Safety Information (CSI). No changes to the protocol or Patient Information Leaflet are required. The benefit/risk profile of the study remains unchanged.
31 October 2019	This substantial amendment to Protocol v 8 (21Jun2019) included an amendment to inclusion criteria: PKI3CA mutation have been removed from the inclusion criteria and patients will be enrolled regardless of their PIK3CA mutation status. The rationale is based on the results of the Phase Ib part of PantHER suggesting that PIK3CA mutation status did not impact on the likelihood of clinical benefit from Copanlisib/Trastuzumab and additional studies that have already been published.

09 September 2020	This substantial amendment to Protocol v9 (27Aug2020) concerns the following key change: - At the time of the PantHER study protocol submission for Clinical Trial Application, Herceptin® (Roche Registration GmbH) was the only brand of trastuzumab approved by the European Medicines Agency. After the patent on Herceptin® expired in Europe in July 2014 this has led to biosimilars of trastuzumab being developed. Currently there are five trastuzumab biosimilars approved in Ireland. Due to the high cost of Herceptin® during the last year, Irish hospitals have been switching to trastuzumab biosimilars to reduce the cost of the cancer patient treatment. Limiting PantHER study patient treatment only to Herceptin® has a significant impact to study accrual and the cost for sites who are treating study patients. As such, the PantHER study protocol has been updated to allow other trastuzumab biosimilars to be used for study patients and give sites more flexibility for patient treatment.
31 January 2022	All patients have finished protocol treatment and continue on the trial in the follow-up phase. The trial protocol has been amended to reduce the long-term follow-up for these patients. According to the amended protocol v10 (21Oct2021), it is planned that survival follow-up will be continued until death or until a maximum of one year after last patient last treatment visit, whichever occurs first. The last patient last treatment visit occurred in February 2021 and long-term follow-up will be completed by February 2022. Due to the small patient sample size, any estimates for overall survival are exploratory. Currently from 26 patients registered on study, 19 patients are now off study. Following up for more than one year is unlikely to provide much more definitive information for the trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported