Clinical trial results:
An Open-Label Phase 2 Study to Characterize Colon Pathology in Patients With HER2 Amplified Breast Cancer Treated With Neratinib

Summary

EudraCT number	2019-001896-35
Trial protocol	PT
Global end of trial date	28 December 2021

Results information

Result version number	v1 (current)
This version publication date	08 January 2023
First version publication date	08 January 2023

Trial information

Trial identification

Sponsor protocol code	PUMA-NER-6203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04366713
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Puma Biotechnology, Inc.
Sponsor organisation address	10880 Wilshire Blvd, Suite 2150, Los Angeles, United States, 90024
Public contact	Clinical Trial Management, Puma Biotechnology, Inc, +1 4242486500, clinicaltrials@pumabiotechnology.com
Scientific contact	Clinical Trial Management, Puma Biotechnology, Inc, +1 4242486500, clinicaltrials@pumabiotechnology.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	31 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2021
Global end of trial reached?	Yes
Global end of trial date	28 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize and understand colon pathogenesis related to neratinib-induced diarrhea through biopsies and images obtained by colonoscopy study.

Protection of trial subjects:

Study commencement required prior written approval of a properly constituted Independent Ethics Committee (IEC). Clinical trial data were monitored at regular intervals by the Sponsor or their representative throughout the study to verify compliance to study protocol, completeness, accuracy and consistency of the data and adherence to local regulations on the conduct of clinical research. Patients were discontinued from investigational product(s) (IP) in the following circumstances: if patient required more than two dose reductions of neratinib, disease recurrence, initiation of alternative anti-cancer therapy, pregnancy, investigator request, patient request, or adverse event/toxicity.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 December 2019
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	Portugal: 6
Worldwide total number of subjects	6
EEA total number of subjects	6

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	1

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening activities are to be conducted within 28 days prior to Cycle 1/Day 1, except for serum or urine pregnancy test for women of child-bearing potential, which should be performed, both, at screening and repeated within 72 hours prior to C1D1. Documentation of locally assessed ERBB2-amplified status by FISH or IHC(3+) must be confirmed.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Neratinib

Arm description:

All treated patients

Arm type	Experimental
Investigational medicinal product name	Neratinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All patients will receive neratinib for the first 28 days as a single daily dose of 240mg. For patients being treated for stage 1 to 3c breast cancer in the extended adjuvant setting, neratinib will continue to be administered at a single daily dose of 240 mg until completion of one year of therapy from start of treatment, or until disease recurrence (as determined by the Investigator), death, unacceptable toxicity, or other specified withdrawal criterion.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

For patients being treated for metastatic breast cancer (mBC), capecitabine will be introduced after the second study colonoscopy procedure at a dose of 750mg/m2 twice daily for 14 days of each 21 day treatment cycle, with neratinib administered continuously throughout at 240mg daily, until disease progression, death, unacceptable toxicity, or other specified withdrawal criterion

Number of subjects in period 1	Neratinib
Started	6
Treated	5
Completed	4
Not completed	2

Ineligible for treatment	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment

Reporting group description: -

Reporting group values	Treatment	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Adults (18-64 years)	5	5	
From 65-84 years	1	1	
Age continuous Units: years			
arithmetic mean	46.3		
standard deviation	± 13.4	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	0	0	

End points

End points reporting groups

Reporting group title	Neratinib
Reporting group description:	
All treated patients	

Primary: Changes in Colon Pathology

End point title	Changes in Colon Pathology[1]
End point description:	
Change from baseline in pathological findings in colon biopsies after the first 28 days of neratinib treatment.	
End point type	Primary
End point timeframe:	
From baseline to 28 days after neratinib treatment	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No formal statistical analyses were planned or conducted. All results are descriptive.	

End point values	Neratinib			
Subject group type	Reporting group			
Number of subjects analysed	4[2]			
Units: Patients				
No changes	2			
Mild changes	2			

Notes:

[2] - Number of patients with two colonocopies

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Severity of Diarrhea

End point title	Incidence and Severity of Diarrhea
End point description:	
End point type	Secondary
End point timeframe:	
For first 28 days of neratinib treatment	

End point values	Neratinib			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Percentage of Patients				
number (not applicable)				
Overall	80			
Serious	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From time of first dose, through 28 days after last dose, assessed up to 16 months.

Adverse event reporting additional description:

Safety population: Participants receiving at least 1 dose of investigational product.
Serious and Non-serious Adverse Events were monitored/assessed only in the safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Neratinib

Reporting group description:

Neratinib

Serious adverse events	Neratinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Pneumonia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Neratinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)		
Investigations			
Platelet count decreased			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 5 (40.00%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed occurrences (all) Faeces hard subjects affected / exposed occurrences (all) Faeces soft subjects affected / exposed occurrences (all) Flatulence subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	5 / 5 (100.00%) 39 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 3 / 5 (60.00%) 4 1 / 5 (20.00%) 2		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Infections and infestations Paronychia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported