Clinical trial results:
Phase II, open label clinical study to investigate anti-tumour effect and tolerability of the PARP inhibitor 2X-121 in patients with metastatic breast cancer selected by the 2X-121 DRP®.

Summary

EudraCT number	2017-003508-39
Trial protocol	DK
Global end of trial date	24 June 2020

Results information

Result version number	v1 (current)
This version publication date	23 June 2024
First version publication date	23 June 2024

Trial information

Trial identification

Sponsor protocol code	SMR-3475

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Allarity Therapeutics Europe AS
Sponsor organisation address	Venlighdsvej 1, Horsholm, Denmark, 2970
Public contact	Marie Foegh, Allarity Therapeutics Europe AS, +45 NA, mfoegh@allarity.com
Scientific contact	Marie Foegh, Allarity Therapeutics Europe AS, +45 NA, mfoegh@allarity.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	17 August 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 June 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the anti-tumour efficacy after treatment with 600 mg 2X-121 as single agent in a 21-days cycle in metastatic breast cancer patients selected by the 2X-121 DRP.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2018
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	Denmark: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	13
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at two sited in Denmark. First patient first visit was 22Jun2018. Last patient last visit was 24Jun2020. A total of 16 subjects were include in the study, of these 14 subjects received treatment.

Pre-assignment

Screening details:

A drug response prediction (DRP) was used as a companion diagnostic for selection of subjects.

Period 1

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

Blinding implementation details:

Open trail

Arms

Arm title	Treatment 2X-121

Arm description:

Every patient will receive daily oral administrations of 3 x 200 mg 2X-121 in a 21 days cycle.

Arm type	Experimental
Investigational medicinal product name	2X-121
Investigational medicinal product code	2X-121
Other name	Stenoparib
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Every patient will receive daily oral administrations of 3 x 200 mg 2X-121 in a 21 days cycle until progression

Number of subjects in period 1	Treatment 2X-121
Started	16
Completed	14
Not completed	2
Screening failure	2

Baseline characteristics

Reporting groups

Reporting group title	Study period

Reporting group description: -

Reporting group values	Study period	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	51.5		
standard deviation	± 13.4	-	
Gender categorical Units: Subjects			
Female	16	16	
Male	0	0	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients would be included in the intention-to-treat (ITT) population for analysis if they had measurable disease at baseline and receive treatment for at least one dose of 2X-121.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

In order to qualify for the stringent per protocol population, patients should follow the study protocol without any major violation, and should receive at least 2 cycles of treatment.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients will be included in the safety population if they have measurable disease at baseline and receive treatment for at least one dose of 2X-121.

Subject analysis set title	Evaluable
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Evaluable population includes PP population and patients with disease progression before completing 2 cycles.

Reporting group values	ITT	Per Protocol	Safety population
Number of subjects	14	14	9
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	51.5	ND	ND
standard deviation	± 13.4	±	±
Gender categorical			
Units: Subjects			
Female	16	14	16
Male	0	0	0

Reporting group values	Evaluable		
Number of subjects	11		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	ND		
standard deviation	±		
Gender categorical			
Units: Subjects			
Female	11		
Male	0		

End points

End points reporting groups

Reporting group title	Treatment 2X-121
Reporting group description:	
Every patient will receive daily oral administrations of 3 x 200 mg 2X-121 in a 21 days cycle.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients would be included in the intention-to-treat (ITT) population for analysis if they had measurable disease at baseline and receive treatment for at least one dose of 2X-121.	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
In order to qualify for the stringent per protocol population, patients should follow the study protocol without any major violation, and should receive at least 2 cycles of treatment.	

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
Patients will be included in the safety population if they have measurable disease at baseline and receive treatment for at least one dose of 2X-121.	
Subject analysis set title	Evaluable
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Evaluable population includes PP population and patients with disease progression before completing 2 cycles.	

Primary: Clinical Benefit Rate (CBR) > 24 weeks

End point title	Clinical Benefit Rate (CBR) > 24 weeks[1]
End point description:	

End point type	Primary
End point timeframe:	
Clinical Benefit Rate (CBR) > 24 weeks	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not available

End point values	Treatment 2X-121	ITT		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	11	14		
Units: Subject (%)				
CR> 24W	0	0		
PR>24W	0	0		
SD>24W	1	1		
CBR>24W	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first administration of IMP

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	All subjects

Reporting group description: -

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 14 (35.71%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Metastases to central nervous system			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Vascular disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Surgical and medical procedures			
Cataract			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
General disorders and administration			

site conditions			
Axillary pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Burning sensation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed	8 / 14 (57.14%)		
occurrences (all)	8		
Disease progression			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	11 / 14 (78.57%)		
occurrences (all)	11		
General physical health deterioration			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	6 / 14 (42.86%)		
occurrences (all)	6		
Non-cardiac chest pain			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Neuralgia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Ear and labyrinth disorders Inner ear disorder subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Eye disorders Photophobia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 3 / 14 (21.43%) 3 6 / 14 (42.86%) 6 1 / 14 (7.14%) 1 8 / 14 (57.14%) 8 1 / 14 (7.14%) 1		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Nail disorder subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 1 / 14 (7.14%) 1		

Photosensitivity reaction subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		
Pruritus subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
pruritus generalised subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Rash subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2		
Rash maculo-papular subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 4		
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all)	13 / 14 (92.86%) 13		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 4		
Bone pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Myalgia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3		
Neck pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Infections and infestations Cystitis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		

Oral candidiasis			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Oral fungal infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2018	Change to inclusion criteria 3 and 11d Add restriction on intake of IMP related to food
24 June 2019	Change in dosing schedule for IMP

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was not completed

Notes: