Clinical trial results:
A Study of BR55 in Contrast Enhanced Ultrasound Imaging in Patients with Ovarian and Breast Cancer.

Summary

EudraCT number	2012-000699-40
Trial protocol	IT
Global end of trial date	02 April 2014

Results information

Result version number	v1 (current)
This version publication date	27 March 2021
First version publication date	27 March 2021

Trial information

Trial identification

Sponsor protocol code	BR55-102

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bracco Diagnostics, Inc.
Sponsor organisation address	259 Prospect Plains Rd, , Cranbury, United States, 08512
Public contact	Global Medical & Regulatory Affairs, Bracco Imaging spa, 609 514-2200,
Scientific contact	Global Medical & Regulatory Affairs, Bracco Imaging spa, 609 514-2200,

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	16 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 April 2014
Global end of trial reached?	Yes
Global end of trial date	02 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess ultrasound imaging results with BR55 in the detection of cancer lesions in patients with ovarian cancer or ovarian mass or patient with breast cancer using histology as the truth standard for the presence/absence of malignant lesions.

Protection of trial subjects:

The safety endpoints for patients enrolled in the preceding (at least 4 patients) dose group were to be completed and reviewed for any unexpected safety risks before proceeding with the enrollment in the next dose group.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 October 2012
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	Italy: 47
Worldwide total number of subjects	47
EEA total number of subjects	47

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)	38
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 25 October 2012
Last patient completed: 2 April 2014

Pre-assignment

Screening details:

Two enrolled patients did not receive drug, one had suspected cardiac ischemia indicated at the predose ECG examination, and one had uncontrolled systemic hypertension at the predose clinical evaluation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ovary Patients

Arm description:

Ovary Patients scheduled to undergo surgery for primary ovarian cancer or ovarian mass

Arm type	Experimental
Investigational medicinal product name	BR55
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Each patient in the 3 dose groups (Group A = 0.03 mL/kg, Group B = 0.05 mL/kg, and Group C = 0.08 mL/kg) received one injection of BR55 at the assigned dose. The maximum dose of BRU2248 for a patient cannot exceed 100 µg and therefore body weight could not be greater than 95 kg in this study. The calculated dose of BR55 was determined by body weight using a dosing calculation guide.
BR55 was administered as a slow intravenous bolus injection through an angiocatheter (20G). Each injection was followed immediately by a 10 mL 0.9% NaCl flush.

Arm title	Breast Patients

Arm description:

Breast Patients scheduled to undergo primary breast cancer surgery or large core biopsy of the breast

Arm type	Experimental
Investigational medicinal product name	BR55
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Each patient in the 3 dose groups (Group A = 0.03 mL/kg, Group B = 0.05 mL/kg, and Group C = 0.08 mL/kg) received one injection of BR55 at the assigned dose. The maximum dose of BRU2248 for a patient cannot exceed 100 µg and therefore body weight could not be greater than 95 kg in this study. The calculated dose of BR55 was determined by body weight using a dosing calculation guide.
BR55 was administered as a slow intravenous bolus injection through an angiocatheter (20G). Each injection was followed immediately by a 10 mL 0.9% NaCl flush.

Number of subjects in period 1[1]	Ovary Patients	Breast Patients
Started	24	21
Completed	24	21

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Two enrolled patients did not receive drug, one had suspected cardiac ischemia indicated at the predose ECG examination, and one had uncontrolled systemic hypertension at the predose clinical evaluation.

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	45	45	
Age categorical Units: Subjects			
Adults (18-64 years)	38	38	
≥65 years	7	7	
Gender categorical Units: Subjects			
Female	45	45	
Male	0	0	

Subject analysis sets	
Subject analysis set title	Ovarian Patients
Subject analysis set type	Full analysis
Subject analysis set description: Ovary Patients scheduled to undergo surgery for primary ovarian cancer or ovarian mass	
Subject analysis set title	Breast Patients
Subject analysis set type	Full analysis
Subject analysis set description: Breast Patients scheduled to undergo primary breast cancer surgery or large core biopsy of the breast	
Subject analysis set title	Patients with Malignant Ovarian Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Malignant Ovarian Lesions	
Subject analysis set title	Patients with Benign Ovarian Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Benign Ovarian Lesionsc	
Subject analysis set title	Patients with Malignant Breast Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Malignant Breast Lesionsb	
Subject analysis set title	Patients with Benign Breast Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Benign Breast Lesionsb	

Reporting group values	Ovarian Patients	Breast Patients	Patients with Malignant Ovarian Lesions
Number of subjects	24	21	13

Age categorical Units: Subjects			
Adults (18-64 years)	18	20	10
≥65 years	6	1	3
Gender categorical Units: Subjects			
Female	24	21	13
Male	0	0	0

Reporting group values	Patients with Benign Ovarian Lesions	Patients with Malignant Breast Lesions	Patients with Benign Breast Lesions
Number of subjects	11	17	4
Age categorical Units: Subjects			
Adults (18-64 years)	8	16	4
≥65 years	3	1	0
Gender categorical Units: Subjects			
Female	11	17	4
Male	0	0	0

End points

End points reporting groups

Reporting group title	Ovary Patients
Reporting group description: Ovary Patients scheduled to undergo surgery for primary ovarian cancer or ovarian mass	
Reporting group title	Breast Patients
Reporting group description: Breast Patients scheduled to undergo primary breast cancer surgery or large core biopsy of the breast	
Subject analysis set title	Ovarian Patients
Subject analysis set type	Full analysis
Subject analysis set description: Ovary Patients scheduled to undergo surgery for primary ovarian cancer or ovarian mass	
Subject analysis set title	Breast Patients
Subject analysis set type	Full analysis
Subject analysis set description: Breast Patients scheduled to undergo primary breast cancer surgery or large core biopsy of the breast	
Subject analysis set title	Patients with Malignant Ovarian Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Malignant Ovarian Lesions	
Subject analysis set title	Patients with Benign Ovarian Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Benign Ovarian Lesionsc	
Subject analysis set title	Patients with Malignant Breast Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Malignant Breast Lesionsb	
Subject analysis set title	Patients with Benign Breast Lesions
Subject analysis set type	Intention-to-treat
Subject analysis set description: Patients with Benign Breast Lesionsb	

Primary: KDR Staining of Index Lesion versus CD31 Staining by Histopathology - Ovary

End point title	KDR Staining of Index Lesion versus CD31 Staining by Histopathology - Ovary[1][2]

End point description:

The number of index lesions with KDR and CD31 staining scores of high, intermediate, or weak by IHC assessment for both malignant and benign ovarian lesions.

Each of the 24 dosed patients had 1 index lesion identified by histopathology. Based on the histopathology analysis, 13 of the 24 (54.2%) index lesions were malignant and 11 (45.8%) lesions were benign.

End point type	Primary

End point timeframe:

Postdose

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: Descriptive statistics are provided in the descriptions of the Primary Endpoint Results. No

other statistical analyses were planned for the efficacy endpoints as the study was exploratory.

[2] - 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: Descriptive statistics are provided in the descriptions of the Primary Endpoint Results. No other statistical analyses were planned for the efficacy endpoints as the study was exploratory.

End point values	Ovary Patients			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Number of Patients				
Patients with Malignant Ovarian Lesions	13			
Patients with Benign Ovarian Lesions	11			

Statistical analyses

No statistical analyses for this end point

Primary: BR55 Enhancement of Index Lesion versus CD31 Staining by Histopathology Using a Dichotomized Scale – Ovary

End point title	BR55 Enhancement of Index Lesion versus CD31 Staining by Histopathology Using a Dichotomized Scale – Ovary[3]

End point description:

BR55 enhancement and CD31 staining of the ovarian index lesions. A BR55 enhancement score of the index lesion according to ultrasound images. BR55 enhancement scores of slight, moderate and strong enhancement were considered as Yes. All index lesions had CD31 staining.

13/13 (100%) malignant lesions had both CD31 staining and BR55 enhancement; among 11 benign lesions with CD31 staining, 9 (81.8%) had BR55 enhancement and 2 did not.

End point type	Primary

End point timeframe:

Postdose

Notes:

[3] - 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: Descriptive statistics are provided in the descriptions of the Primary Endpoint Results. No other statistical analyses were planned for the efficacy endpoints as the study was exploratory.

End point values	Patients with Malignant Ovarian Lesions	Patients with Benign Ovarian Lesions		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	11		
Units: Lesions				
number (not applicable)				
No	0	2		
Yes	13	9		
Total	13	11		

Statistical analyses

No statistical analyses for this end point

Primary: KDR Staining of Index Lesion versus CD31 Staining by Histopathology - Breast

End point title	KDR Staining of Index Lesion versus CD31 Staining by Histopathology - Breast[4][5]

End point description:

The number of index lesions with KDR and CD31 staining scores of high, intermediate, or weak by IHC assessment for both malignant and benign breast lesions.

Each of the 21 dosed patients had 1 index lesion identified by histopathology. Based on the histopathology analysis, 17 of 21 (81.0%) index lesions were malignant and 4 (19.0%) index lesions were benign.

End point type	Primary

End point timeframe:

Postdose

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: Descriptive statistics are provided in the descriptions of the Primary Endpoint Results. No other statistical analyses were planned for the efficacy endpoints as the study was exploratory.
[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: Descriptive statistics are provided in the descriptions of the Primary Endpoint Results. No other statistical analyses were planned for the efficacy endpoints as the study was exploratory.

End point values	Breast Patients			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Lesions				
number (not applicable)				
Patients with Malignant Breast Lesions	17			
Patients with Benign Breast Lesions	4			

Statistical analyses

No statistical analyses for this end point

Primary: BR55 Enhancement of Index Lesion versus CD31 Staining by Histopathology Using a Dichotomized Scale – Breast

End point title	BR55 Enhancement of Index Lesion versus CD31 Staining by Histopathology Using a Dichotomized Scale – Breast[6]

End point description:

BR55 enhancement and CD31 staining of the breast index lesions. A BR55 enhancement score of the index lesion according to ultrasound images. BR55 enhancement scores of slight, moderate and strong enhancement were considered as Yes. All index lesions had CD31 staining.

16/17 (94.1%) malignant lesions had both CD31 staining and BR55 enhancement and among the 4 benign lesions with CD31 staining, 2 lesions (50.0%) had BR55 enhancement and 2 (50.0%) had none.

End point type	Primary

End point timeframe:

Postdose

Notes:

[6] - 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: Descriptive statistics are provided in the descriptions of the Primary Endpoint Results. No other statistical analyses were planned for the efficacy endpoints as the study was exploratory.

End point values	Patients with Malignant Breast Lesions	Patients with Benign Breast Lesions		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	4		
Units: Lesions				
number (not applicable)				
No	1	2		
Yes	16	2		
Total	17	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Patients were monitored for any untoward medical occurrences from the time of signing the Informed Consent through 72 hours after BR55 administration

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Ovarian
Reporting group description: -	
Reporting group title	Breast

Reporting group description: -

Serious adverse events	Ovarian	Breast	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 21 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Ovarian	Breast	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 24 (20.83%)	7 / 21 (33.33%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 24 (4.17%)	1 / 21 (4.76%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 24 (4.17%)	6 / 21 (28.57%)	
occurrences (all)	1	6	
Gastrointestinal disorders			
Lip pruritus			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Oral discomfort			
subjects affected / exposed	0 / 24 (0.00%)	1 / 21 (4.76%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	1 / 24 (4.17%)	0 / 21 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 24 (8.33%)	0 / 21 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 January 2013	The inclusion criteria was amended to also allow perimenopausal females to enroll, provided that they met the enrollment criteria and were not pregnant or breast-feeding.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported