Clinical trial results:
CORALLEEN: A Phase 2 Clinical Trial of multi-agent Chemotherapy or letrozole plus Ribociclib (LEE001) as neoadjuvant treatment for postmenopausal patients with Luminal B/HER2-negative breast cancer.

Summary

EudraCT number	2016-003098-17
Trial protocol	ES
Global end of trial date	01 July 2019

Results information

Result version number	v1 (current)
This version publication date	27 April 2022
First version publication date	27 April 2022
Summary attachment (see zip file)	SOLTI-1402_SYNOPSIS CSR (SOLTI-1402_SYNOPSIS CSR v1.0_20200608_EN.pdf)

Trial information

Trial identification

Sponsor protocol code	SOLTI-1402

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03248427
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SOLTI
Sponsor organisation address	C/ Balmes 89 3-7, Barcelona, Spain, 08008
Public contact	Investigación Clínica, SOLTI, 34 933436302, regsolti@gruposolti.org
Scientific contact	Investigación Clínica, SOLTI, 34 933436302, regsolti@gruposolti.org

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	08 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2019
Global end of trial reached?	Yes
Global end of trial date	01 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the clinical benefit of ribociclib plus letrozole versus chemotherapy.

Protection of trial subjects:

All patients received written and verbal information regarding the study at a prior interview with investigator site staff. This information will emphasised that participation in the study is voluntary and that the subject may withdraw from the study at any time and for any reason. All patients were given the opportunity to ask questions about the study and were given sufficient time to decide whether to participate.The IC mentioned which specific data was recorded, collected, processed and could be transferred to European Economic Area (EEA) or non-EEA countries. Personal data was managed in accordance with the applicable legislation in force at the time, and in particular, in accordance with Regulation (EU) No 2016/679 of 27 April 2016 on the protection of individuals with regard to the processing of their personal data (hereinafter, "GDPR"). A copy of the patient information including the signed IC form was provided to the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 2017
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	Spain: 106
Worldwide total number of subjects	106
EEA total number of subjects	106

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)	53
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Planned: 94 patients to be recruited. Considering 10% drop-out rate, 104 patients was planned to be included.From July 27, 2017 to December 7, 2018, 198 patients were assessed for eligibility across 21 centres in Spain and 106 were finally recruited.

Pre-assignment

Screening details:

Postmenopausal women with untreated primary operable Hormone receptor positive (HR+)/HER2-negative Luminal B breast cancer according to PAM50 intrinsic subtype

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	letrozole plus ribociclib

Arm description:

The letrozole plus ribociclib treatment consisted of six 28-days cycles of daily letrozole (2.5mg; continuous) and ribociclib (600mg; 3-weeks-on/-week-off).
The study investigational treatment was Ribociclib (Kisqali ®) provided by Novartis. It was administered as a flat-fixed dose of 600 mg daily (three 200-mg capsules), days 1 to 21 of a 28-days cycle.
Letrozole (Femara®) was also supplied by Novartis. Letrozole was administered orally, once per day, days 1 to 28 of a 28 days cycle, at 2.5 mg. Both ribociclib and letrozole were administered orally during 6 cycles and independently of the body surface area or body weight.
The ribociclib destined for use in the trial came from batches 1010010567 and WX027; and letrozole from batch SH083

Arm type	Experimental
Investigational medicinal product name	Ribociclib (Kisqali®)
Investigational medicinal product code	L01EF02
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Ribociclib was administered as a flat-fixed dose of 600 mg daily (three 200-mg capsules), days 1 to 21 of a 28-days cycle during 6 cycles.

Investigational medicinal product name	Letrozole
Investigational medicinal product code	L02BG04
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Letrozole (Femara®) was also supplied by Novartis. Letrozole was administered once per day, days 1 to 28 of a 28 days cycle, at 2.5 mg.

Arm title	Chemotherapy

Arm description:

The chemotherapy treatment consisted of four cycles of AC (doxorubicin 60 mg/m2 and cyclophosphamide 600 mg/m2 every21 days) followed by weekly paclitaxel during 12 weeks. In total, neoadjuvant therapy lasted for 24 weeks in each arm.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	letrozole plus ribociclib	Chemotherapy
Started	52	54
Completed	43	42
Not completed	9	12
Consent withdrawn by subject	1	2
Adverse event, non-fatal	8	10

Baseline characteristics

Reporting groups	
Reporting group title	letrozole plus ribociclib
Reporting group description:	
The letrozole plus ribociclib treatment consisted of six 28-days cycles of daily letrozole (2.5mg; continuous) and ribociclib (600mg; 3-weeks-on/-week-off). The study investigational treatment was Ribociclib (Kisqali ®) provided by Novartis. It was administered as a flat-fixed dose of 600 mg daily (three 200-mg capsules), days 1 to 21 of a 28-days cycle. Letrozole (Femara®) was also supplied by Novartis. Letrozole was administered orally, once per day, days 1 to 28 of a 28 days cycle, at 2.5 mg. Both ribociclib and letrozole were administered orally during 6 cycles and independently of the body surface area or body weight. The ribociclib destined for use in the trial came from batches 1010010567 and WX027; and letrozole from batch SH083	
Reporting group title	Chemotherapy
Reporting group description:	
The chemotherapy treatment consisted of four cycles of AC (doxorubicin 60 mg/m2 and cyclophosphamide 600 mg/m2 every21 days) followed by weekly paclitaxel during 12 weeks. In total, neoadjuvant therapy lasted for 24 weeks in each arm.	

Reporting group values	letrozole plus ribociclib	Chemotherapy	Total
Number of subjects	52	54	106
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			
The baseline median age was 63.5 years (range 49-79)			
Units: years			
median	63	64	
full range (min-max)	50 to 78	49 to 79	-
Gender categorical Units: Subjects			
Female	52	54	106
Male	0	0	0
Tumor size Units: Subjects			
T1	3	3	6
T2	40	43	83
T3	9	8	17
Lymph node status Units: Subjects			
N0	31	31	62

N1	19	22	41
N2	2	1	3
Histological type Units: Subjects			
Ductal	41	48	89
Lobular	10	6	16
Other	1	0	1
Clinical baseline tumour stage Units: Subjects			
One	2	2	4
Two	43	45	88
Three	7	7	14
PR expression > 20% Units: Subjects			
PR expression >20%	18	16	34
PR expression < 20 %	34	38	72
Ki67 expression (local) Units: Subjects			
≤14%	3	2	5
>14%	49	51	100
Missing	0	1	1
PR-negative Units: Subjects			
PR-negative	11	9	20
Other	41	45	86
Median ROR score Units: Range			
median	70	77	
full range (min-max)	52 to 93	51 to 97	-
Mean ROR score Units: Mean			
arithmetic mean	71.5	74.2	
standard deviation	± 9.85	± 10.7	-
Ki67 expression mean Units: Mean			
arithmetic mean	31.1	35.2	
standard deviation	± 13.64	± 12.6	-
Ki67 expression (range) Units: Median			
median	30	35	
full range (min-max)	5 to 75	12 to 70	-

Subject analysis sets

Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT population was defined as all randomized patients	
Subject analysis set title	modified ITT (mITT) population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified ITT (mITT) population was defined as all randomized patients who received study medication and had a baseline efficacy measurement and at least one corresponding postbaseline efficacy measurement (for the main efficacy variable).

Subject analysis set title	Per Protocol (PP) population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) population was defined as all randomized subjects who met the inclusion criteria, received study medication, had a baseline efficacy measurement and at least one corresponding post-baseline efficacy measurement (for the main efficacy variable) and did not present major violations of the protocol.

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

Subject analysis set description:

The Safety population defined as all randomized subjects who took at least one dose of the study medication

Reporting group values	ITT population	modified ITT (mITT) population	Per Protocol (PP) population
Number of subjects	103	101	88
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			
The baseline median age was 63.5 years (range 49-79)			
Units: years median full range (min-max)	 63.5 49 to 79		
Gender categorical Units: Subjects			
Female Male	106 0		
Tumor size Units: Subjects			
T1 T2 T3	6 83 17		
Lymph node status Units: Subjects			
N0 N1 N2	62 41 3		
Histological type Units: Subjects			

Ductal	89		
Lobular	16		
Other	1		
Clinical baseline tumour stage Units: Subjects			
One	4		
Two	88		
Three	14		
PR expression > 20% Units: Subjects			
PR expression >20%	34		
PR expression < 20 %			
Ki67 expression (local) Units: Subjects			
≤14%	5		
>14%	100		
Missing	1		
PR-negative Units: Subjects			
PR-negative			
Other			
Median ROR score Units: Range			
median	74.5		
full range (min-max)	51 to 97		
Mean ROR score Units: Mean			
arithmetic mean	72.9		
standard deviation	± 10.3	±	±
Ki67 expression mean Units: Mean			
arithmetic mean	33.1		
standard deviation	± 13.2	±	±
Ki67 expression (range) Units: Median			
median	32		
full range (min-max)	5 to 75		

Reporting group values	Safety population		
Number of subjects	103		
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			
The baseline median age was 63.5 years (range 49-79)			
Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Female Male			
Tumor size Units: Subjects			
T1 T2 T3			
Lymph node status Units: Subjects			
N0 N1 N2			
Histological type Units: Subjects			
Ductal Lobular Other			
Clinical baseline tumour stage Units: Subjects			
One Two Three			
PR expression > 20% Units: Subjects			
PR expression >20% PR expression < 20 %			
Ki67 expression (local) Units: Subjects			
≤14% >14% Missing			
PR-negative Units: Subjects			
PR-negative Other			
Median ROR score Units: Range median full range (min-max)			
Mean ROR score Units: Mean			

arithmetic mean standard deviation	±		
Ki67 expression mean Units: Mean arithmetic mean standard deviation	±		
Ki67 expression (range) Units: Median median full range (min-max)			

End points

End points reporting groups

Reporting group title	letrozole plus ribociclib

Reporting group description:

The letrozole plus ribociclib treatment consisted of six 28-days cycles of daily letrozole (2.5mg; continuous) and ribociclib (600mg; 3-weeks-on/-week-off).
The study investigational treatment was Ribociclib (Kisqali ®) provided by Novartis. It was administered as a flat-fixed dose of 600 mg daily (three 200-mg capsules), days 1 to 21 of a 28-days cycle.
Letrozole (Femara®) was also supplied by Novartis. Letrozole was administered orally, once per day, days 1 to 28 of a 28 days cycle, at 2.5 mg. Both ribociclib and letrozole were administered orally during 6 cycles and independently of the body surface area or body weight.
The ribociclib destined for use in the trial came from batches 1010010567 and WX027; and letrozole from batch SH083

Reporting group title	Chemotherapy

Reporting group description:

The chemotherapy treatment consisted of four cycles of AC (doxorubicin 60 mg/m2 and cyclophosphamide 600 mg/m2 every21 days) followed by weekly paclitaxel during 12 weeks. In total, neoadjuvant therapy lasted for 24 weeks in each arm.

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

Subject analysis set description:

The ITT population was defined as all randomized patients

Subject analysis set title	modified ITT (mITT) population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The modified ITT (mITT) population was defined as all randomized patients who received study medication and had a baseline efficacy measurement and at least one corresponding postbaseline efficacy measurement (for the main efficacy variable).

Subject analysis set title	Per Protocol (PP) population
Subject analysis set type	Per protocol

Subject analysis set description:

The Per Protocol (PP) population was defined as all randomized subjects who met the inclusion criteria, received study medication, had a baseline efficacy measurement and at least one corresponding post-baseline efficacy measurement (for the main efficacy variable) and did not present major violations of the protocol.

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

Subject analysis set description:

The Safety population defined as all randomized subjects who took at least one dose of the study medication

Primary: To evaluate the ability of each treatment strategy to provide ROR-low score at surgery

End point title	To evaluate the ability of each treatment strategy to provide ROR-low score at surgery

End point description:

The primary endpoint was to evaluate the rate of ROR-low disease after neoadjuvant treatment (i.e. at surgery) according to the standardized PAM50 assay. ROR score is based on information coming from gene expression data and tumour size and has a range from 0 to 100.
ROR-low disease was defined as ≤40 points if node-negative and ≤15 points if 1-3 positive nodes. ROR-intermediate disease was defined as 41-60 points if node-negative and 16-40 points if 1-3 positive nodes. ROR-high disease was defined as 61-100 points if node-negative
and 41-100 points if 1-3 positive nodes. All patients with ≥4 node positives were considered ROR-high risk regardless of ROR score.

End point type	Primary

End point timeframe:

ROR score was determined at surgery

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Subjects				
ROR-low disease	23	24		
ROR-intermediate disease	15	16		
ROR-high disease	11	11		
Missing	0	1		

Statistical analyses

Statistical analysis title	Estimation of ROR-low rates

Statistical analysis description:

Main analysis is the estimation of ROR-low rates and was described by means of difference of proportions and 95% confidence interval using exact methods based on binomial, ClopperPearson method independently in both treatments groups.
This analysis was performed using ITT approach on ADO data. This primary efficacy analysis was also analyzed using the PP set to test the robustness of the results with the same approach (ADO data)

Comparison groups	letrozole plus ribociclib v Chemotherapy
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	
P-value	≤ 0.05 [1]
Method	Clopper-Pearson
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided

Notes:

[1] - All statistical tests were applied with a 0.05 two-sided significance level.

Secondary: Ki67 (central)

End point title	Ki67 (central)

End point description:

Consistent with the primary results were the results obtained with Ki67 at surgery (Table 10).
The correlation coefficients between ROR score at surgery (as a continuous variable) and Ki67 immunohistochemistry (IHC) expression was 15.4 in the chemotherapy arm and 8.4 in the ribociclib plus letrozole arm.

End point type	Secondary

End point timeframe:

At surgery

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Ki67 immunohistochemistry (IHC) express				
median (full range (min-max))	3 (1 to 70)	10 (1 to 90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Ki67 (central)

End point title	Ki67 (central)

End point description:

End point type	Secondary

End point timeframe:

At surgery

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Ki67 immunohistochemistry (IHC) express				
arithmetic mean (standard deviation)	8.4 (± 13.6)	15.4 (± 17.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by MRI

End point title	ORR by MRI

End point description:

ORR by physical examination, mammography and breast US, if available. Clinical response was evaluated. All patients who have received at least one treatment and have their disease re-evaluated, either by physical examination, US or by MRI, was assigned a response category according to RECIST 1.1 (CR, PR, SD or PD).
Tumor overall objective response rate (ORR) was defined as the sum of Partial Responses (PR) and Complete Responses (CR) according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Breast MRI at screening period and pre-surgery visit at the end of the neoadjuvant treatment

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Subjects				
CR	7	10		
PR	21	31		
SD	16	7		
PD	0	0		
NA	5	3		

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by physical examination

End point title	ORR by physical examination

End point description:

ORR by physical examination, mammography and breast US, if available. Clinical response was evaluated. All patients who have received at least one treatment and have their disease re-evaluated, either by physical examination, US or by MRI, was assigned a response category according to RECIST 1.1 (CR, PR, SD or PD).

End point type	Secondary

End point timeframe:

At screening visit and pre-surgery visit at the end of the neoadjuvant treatment

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Subjects				
CR	16	16		
PR	15	12		
SD	8	5		
PD	1	3		
NA	9	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of pCR

End point title	Rate of pCR

End point description:

pCR in the breast and pCR in the breast and axillary lymph nodes at surgery.
Rate of pCR after neaodjuvant treatment. Pathological complete response (pCR) was evaluated in local laboratories according to two different criteria:
- pCRB defined as the complete absence of invasive cancer in the breast at the time of the definitive surgery, regardless of axillary status or presence of carcinoma in situ (CIS), according to the NSABP definition and guidelines (ypT0/Tis). The presence or absence of CIS was documented.
- pCRBL defined as the complete absence of invasive cancer in the breast and lymph nodes at the time of the definitive surgery (ypT0/Tis, ypN0).

End point type	Secondary

End point timeframe:

at surgery

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Subjects				
Yes	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Residual Cancer Burden (RCB)

End point title	Residual Cancer Burden (RCB)

End point description:

End point type	Secondary

End point timeframe:

At surgery

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Subjects				
0-1	3	6		
II-III	46	45		

Statistical analyses

No statistical analyses for this end point

Secondary: Preoperative endocrine prognostic index (PEPI) score

End point title	Preoperative endocrine prognostic index (PEPI) score

End point description:

Preoperative endocrine prognostic index (PEPI) score in the ribociclib plus letrozole treatment arm compared to historical values. In addition, the PEPI score of surgery samples was determined in patients assigned to the ribociclib-letrozole treatment arm, comparing them to historical values of neoadjuvant letrozole treatment. Both assessments were performed in the central laboratory.

End point type	Secondary

End point timeframe:

Preoperative and surgery samples

End point values	letrozole plus ribociclib	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	52		
Units: Subjects				
zero	11	9		
1-3	25	24		
>4	13	17		
Missing	0	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessment of adverse events and general safety was collected at post-surgery visit. Patients withdrawn from the study before surgery attended to a last follow-up visit 30 days after the administration of the last treatment dose.

Adverse event reporting additional description:

Incidence, duration and severity of Adverse Events (AEs) assessed by the NCI Common Terminology for Classification of Adverse Events (CTCAE) version 4.03, including dose reductions, delays and treatment discontinuations.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	letrozole plus ribociclib

Reporting group description:

The letrozole plus ribociclib treatment consisted of six 28-days cycles of daily letrozole (2.5mg; continuous) and ribociclib (600mg; 3-weeks-on/-week-off).
The study investigational treatment was Ribociclib (Kisqali ®) provided by Novartis. It was administered as a flat-fixed dose of 600 mg daily (three 200-mg capsules), days 1 to 21 of a 28-days cycle.
Letrozole (Femara®) was also supplied by Novartis. Letrozole was administered orally, once per day, days 1 to 28 of a 28 days cycle, at 2.5 mg. Both ribociclib and letrozole were administered orally during 6 cycles and independently of the body surface area or body weight.
The ribociclib destined for use in the trial came from batches 1010010567 and WX027; and letrozole from batch SH083

Reporting group title	Chemotherapy

Reporting group description:

The chemotherapy treatment consisted of four cycles of AC (doxorubicin 60 mg/m2 and cyclophosphamide 600 mg/m2 every21 days) followed by weekly paclitaxel during 12 weeks. In total, neoadjuvant therapy lasted for 24 weeks in each arm.

Serious adverse events	letrozole plus ribociclib	Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 51 (3.92%)	8 / 52 (15.38%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 51 (3.92%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 51 (0.00%)	6 / 52 (11.54%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung abscess			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	1 / 1	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	letrozole plus ribociclib	Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 51 (100.00%)	52 / 52 (100.00%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	2 / 51 (3.92%)	2 / 52 (3.85%)	
occurrences (all)	3	3	
Venous thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	13 / 51 (25.49%)	28 / 52 (53.85%)	
occurrences (all)	18	43	
Axillary pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Chills			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Extravasation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	7 / 51 (13.73%)	10 / 52 (19.23%)	
occurrences (all)	11	32	
Hot flush			
subjects affected / exposed	7 / 51 (13.73%)	0 / 52 (0.00%)	
occurrences (all)	8	0	
Influenza like illness			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Medical device site erythema			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Mucosal dryness			
subjects affected / exposed	4 / 51 (7.84%)	3 / 52 (5.77%)	
occurrences (all)	6	4	
Mucosal inflammation			
subjects affected / exposed	5 / 51 (9.80%)	18 / 52 (34.62%)	
occurrences (all)	6	31	
Oedema peripheral			
subjects affected / exposed	0 / 51 (0.00%)	3 / 52 (5.77%)	
occurrences (all)	0	3	
Pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 51 (0.00%)	3 / 52 (5.77%)	
occurrences (all)	0	4	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	2	0	

Reproductive system and breast disorders			
Adnexa uteri pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Breast pain			
subjects affected / exposed	2 / 51 (3.92%)	1 / 52 (1.92%)	
occurrences (all)	2	1	
Dysmenorrhoea			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal dryness			
subjects affected / exposed	2 / 51 (3.92%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Catarrh			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	4 / 51 (7.84%)	4 / 52 (7.69%)	
occurrences (all)	6	5	
Dysphonia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	2 / 51 (3.92%)	2 / 52 (3.85%)	
occurrences (all)	2	2	
Epistaxis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Nasal dryness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Nasal inflammation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Nasopharyngitis			

subjects affected / exposed	0 / 51 (0.00%)	4 / 52 (7.69%)	
occurrences (all)	0	5	
Productive cough			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	3 / 51 (5.88%)	4 / 52 (7.69%)	
occurrences (all)	5	5	
Respiratory tract infection viral			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences (all)	2	1	
Depression			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	2 / 51 (3.92%)	6 / 52 (11.54%)	
occurrences (all)	2	7	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 51 (25.49%)	4 / 52 (7.69%)	
occurrences (all)	35	5	
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 51 (21.57%)	5 / 52 (9.62%)	
occurrences (all)	20	6	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Blood bilirubin increased			

subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)		
occurrences (all)	1	0		
Blood calcium decreased				
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)		
occurrences (all)	1	0		
Blood chloride increased				
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)		
occurrences (all)	0	1		
Blood cholesterol increased				
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)		
occurrences (all)	1	3		
Blood creatine increased				
subjects affected / exposed	2 / 51 (3.92%)	0 / 52 (0.00%)		
occurrences (all)	2	0		
Blood glucose increased				
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)		
occurrences (all)	0	1		
Blood phosphorus increased				
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)		
occurrences (all)	1	0		
Blood triglycerides increased				
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)		
occurrences (all)	1	0		
Electrocardiogram QT prolonged				
subjects affected / exposed	2 / 51 (3.92%)	0 / 52 (0.00%)		
occurrences (all)	3	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)		
occurrences (all)	1	2		
Lipase increased				
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)		
occurrences (all)	1	1		
Lymphocyte count decreased				
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)		
occurrences (all)	0	1		

Neutrophil count decreased			
subjects affected / exposed	11 / 51 (21.57%)	16 / 52 (30.77%)	
occurrences (all)	33	26	
Platelet count decreased			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Platelet count increased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	2 / 51 (3.92%)	0 / 52 (0.00%)	
occurrences (all)	3	0	
Weight decreased			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	4 / 51 (7.84%)	5 / 52 (9.62%)	
occurrences (all)	8	10	
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Joint dislocation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Cardiac disorders			
Chest pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Ventricular tachycardia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Nervous system disorders			
Disturbance in attention			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	

Dizziness			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	6	
Headache			
subjects affected / exposed	4 / 51 (7.84%)	3 / 52 (5.77%)	
occurrences (all)	6	5	
Hypoaesthesia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	1 / 51 (1.96%)	21 / 52 (40.38%)	
occurrences (all)	1	27	
Neurotoxicity			
subjects affected / exposed	0 / 51 (0.00%)	10 / 52 (19.23%)	
occurrences (all)	0	17	
Paraesthesia			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences (all)	1	3	
Presyncope			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	2	
Vertigo			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 51 (7.84%)	18 / 52 (34.62%)	
occurrences (all)	7	28	
Febrile neutropenia			
subjects affected / exposed	0 / 51 (0.00%)	7 / 52 (13.46%)	
occurrences (all)	0	9	
Leukopenia			

subjects affected / exposed	1 / 51 (1.96%)	2 / 52 (3.85%)	
occurrences (all)	5	2	
Neutropenia			
subjects affected / exposed	17 / 51 (33.33%)	19 / 52 (36.54%)	
occurrences (all)	69	29	
Thrombocytopenia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Haemoglobin decreased			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	3	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences (all)	1	1	
Tinnitus			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences (all)	1	1	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences (all)	2	3	
Dry eye			
subjects affected / exposed	2 / 51 (3.92%)	3 / 52 (5.77%)	
occurrences (all)	3	3	
Hordeolum			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Keratitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	1 / 51 (1.96%)	2 / 52 (3.85%)	
occurrences (all)	1	2	
Vision blurred			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Xerophthalmia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 51 (7.84%)	2 / 52 (3.85%)	
occurrences (all)	6	3	
Abdominal pain lower			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 51 (0.00%)	4 / 52 (7.69%)	
occurrences (all)	0	4	
Anal fissure			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Colitis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	6 / 51 (11.76%)	13 / 52 (25.00%)	
occurrences (all)	7	22	
Dental caries			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	7 / 51 (13.73%)	14 / 52 (26.92%)	
occurrences (all)	16	19	
Dry mouth			
subjects affected / exposed	2 / 51 (3.92%)	5 / 52 (9.62%)	
occurrences (all)	2	7	
Dysgeusia			
subjects affected / exposed	2 / 51 (3.92%)	14 / 52 (26.92%)	
occurrences (all)	2	17	

Dyspepsia			
subjects affected / exposed	4 / 51 (7.84%)	4 / 52 (7.69%)	
occurrences (all)	5	6	
Dysphagia			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences (all)	1	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	2	
Haemorrhoids			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Odynophagia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	0 / 51 (0.00%)	5 / 52 (9.62%)	
occurrences (all)	0	7	
Vomiting			
subjects affected / exposed	2 / 51 (3.92%)	9 / 52 (17.31%)	
occurrences (all)	2	10	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	12 / 51 (23.53%)	33 / 52 (63.46%)	
occurrences (all)	12	43	
Dermatitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Dry skin			

subjects affected / exposed	0 / 51 (0.00%)	3 / 52 (5.77%)	
occurrences (all)	0	5	
Eczema			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Erythema			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences (all)	1	4	
Hand dermatitis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Nail discolouration			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Nail disorder			
subjects affected / exposed	0 / 51 (0.00%)	4 / 52 (7.69%)	
occurrences (all)	0	4	
Nail dystrophy			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Nail infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Nail toxicity			
subjects affected / exposed	0 / 51 (0.00%)	5 / 52 (9.62%)	
occurrences (all)	0	5	
Onycholysis			
subjects affected / exposed	1 / 51 (1.96%)	11 / 52 (21.15%)	
occurrences (all)	1	12	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 51 (1.96%)	3 / 52 (5.77%)	
occurrences (all)	1	3	
Pruritus			
subjects affected / exposed	8 / 51 (15.69%)	4 / 52 (7.69%)	
occurrences (all)	9	6	

Rash			
subjects affected / exposed	12 / 51 (23.53%)	10 / 52 (19.23%)	
occurrences (all)	17	11	
Rash maculo-papular			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Scar pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Skin reaction			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences (all)	1	1	
Toxic skin eruption			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	2 / 51 (3.92%)	2 / 52 (3.85%)	
occurrences (all)	2	2	
Urticaria			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Micturition urgency			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Polyuria			

subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Renal failure			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	3 / 51 (5.88%)	3 / 52 (5.77%)	
occurrences (all)	3	3	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 51 (9.80%)	0 / 52 (0.00%)	
occurrences (all)	5	0	
Back pain			
subjects affected / exposed	2 / 51 (3.92%)	3 / 52 (5.77%)	
occurrences (all)	2	3	
Bone pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Flank pain			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	7 / 51 (13.73%)	4 / 52 (7.69%)	
occurrences (all)	8	5	
Myalgia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Neck pain			

subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	2 / 51 (3.92%)	0 / 52 (0.00%)	
occurrences (all)	2	0	
Sciatica			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Cellulitis			
subjects affected / exposed	0 / 51 (0.00%)	3 / 52 (5.77%)	
occurrences (all)	0	3	
Gingivitis			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Herpes ophthalmic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Infected seroma			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Lip infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Localised infection			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Lung abscess			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Mastitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	

Oral candidiasis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Vulvitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Wound infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Cell death			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	4 / 51 (7.84%)	11 / 52 (21.15%)	
occurrences (all)	4	17	
Dehydration			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	
Hypercholesterolaemia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 52 (3.85%)	
occurrences (all)	0	2	
Hyperglycaemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2017	Amendment number 1 to the protocol (versión 2.0 27 Apr 2017) The amendment consisted of: 1) The addition of plasma sample collection for biomarker analyses Due to the prevalence of the mutations measured at baseline and post treatment and the leves of ctDNA measured in three time.points may provide information on response or resistance to therapy. 2) Expansion to the number of sites: one site was added. 3) Corrections and minor changes 4) Update in the background in reference to clinical trials (MONALEESA 2) 5) Unification of the Prescreening with the Main Informed Consent
15 June 2018	Amendment number 2 to the protocol (Version 3.0 15 June 2018) 1) Change of primary objective and endpoint of the study. 2) Clarify and/or amend of the secondary objectives/endpoints. 3) Clarify/amend some analytical determinations and procedures during the study. 4) Clarify/amend procedures and timelines in Schedule of assessments, especially in reference to the window of collection of tumor sample, randomization and between last dose of ribociclib and surgery. 5) Minor changes as grammatical, typographical and administrative corrections, as well as the addition of new references.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31838010