ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 11/05/2014

ClinicalTrials.gov ID: NCT00559754

Study Identification

Unique Protocol ID:	ML20382
Brief Title:	A Study of Avastin (Bevacizumab) and Sequential Chemotherapy in Patients With Primary HER2 Negative Operable Breast Cancer.
Official Title:	An Open Label Study to Assess the Effect of a Combination of Avastin and Docetaxel and Sequential Chemotherapy on Pathological Response in Patients With Primary Operable HER2 Negative Breast Cancer
Secondary IDs:	

Study Status

Record Verification:	November 2014
Overall Status:	Completed
Study Start:	December 2007
Primary Completion:	September 2010 [Actual]
Study Completion:	September 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: Unknown Board Name: Comite Autonomico de Ensayos Clinicos de Andalucia Board Affiliation: Unknown Phone: +34955006556 Email: mangeles.rasero.sspa@juntadeandalucia.es;
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Spain: Agencia Espanola del medicamento (AEM)

Study Description

Brief Summary:	This single arm study will assess the efficacy and safety of a combination of Avastin and docetaxel following cyclophosphamide and doxorubicin, in patients with HER2 negative operable breast cancer. Patients will receive 4 x 3 week cycles of chemotherapy with doxorubicin (60mg/m2 iv on day 1 of each cycle) and cyclophosphamide (600mg/m2 iv on day 1 of each cycle). They will then receive 4 x 3 week cycles of docetaxel (75mg/m2 on day 1 of each cycle) in combination with Avastin (15mg/kg on day 1 of each cycle). The anticipated time on study treatment is 3-12 months, and the target sample size is <100 individuals.
Detailed Description:	

Conditions

Conditions:	Breast Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 72 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: bevacizumab [Avastin] 15mg/kg iv on day 1 of each 3 week cycle Drug: Docetaxel 75mg/m2 iv on day 1 of each 3 week cycle Drug: Standard chemotherapy As prescribed

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- female patients, >=18 years of age;
- primary HER2-negative operable breast cancer;
- tumor >2cm in size;
- ECOG performance status 0-1.

Exclusion Criteria:

- previous treatment for breast cancer;
- metastatic disease;
- current or recent (within 10 days of first dose of Avastin) use of aspirin (>325mg/day) or full-dose anticoagulants for therapeutic purposes;
- clinically significant cardiovascular disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director

Hoffmann-La Roche

Locations: Spain
Zaragoza, Zaragoza, Spain, 50009

Lerida, Lerida, Spain, 25198

Jaen, Jaen, Spain, 23007

Sabadell, Barcelona, Barcelona, Spain, 08208

Cordoba, Cordoba, Spain, 14004

Malaga, Malaga, Spain, 29010

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 milligrams per square meter (mg/m^2) intravenously (IV) followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg per kilogram (mg/kg) IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Overall Study

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Started	72
Completed	61

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Not Completed	11
Disease progression	1
Adverse Event	5
Protocol Violation	1
Investigator criteria	2
Withdrawal by Subject	2

Baseline Characteristics

Analysis Population Description

Intent to Treat (ITT) Population: all participants included in the study.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Baseline Measures

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants	72
Age, Continuous [units: years] Mean (Standard Deviation)	47.22 (9.85)
Gender, Customized Female [units: participants]	72

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Pathological Complete Response (pCR)

Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria: 1) the primary tumor was Grade 5 (no malignant cells identified at the location of the primary tumor (ductal carcinoma in situ may be present); 2) no involvement was identified in the lymph nodes; 3) the tumour size at evaluation of the surgical piece was 0 centimeters (cm); and 4) the pathological staging of the tumour from the surgical piece was pT0pN0pM0, the stage is not applicable (NA). It will only be considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes.
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Population evaluable for anatomopathological response: participants who satisfied all inclusion criteria and none of the exclusion criteria, received at least 2 cycles of chemotherapy treatment, and were evaluated pathologically.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	66
Percentage of Participants With Pathological Complete Response (pCR) [units: percentage of participants] Number (95% Confidence Interval)	24.2 (14.5 to 36.4)

2. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Objective Clinical Response

Measure Description	Overall clinical response is the best response obtained through physical examination and/or radiological tests after completion of chemotherapy cycles. The percentage of participants with objective response based on assessment of complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumors (RECIST) and was categorized as clinical response (CR+PR) or clinical benefit (CR+PR+ no change [NC]). Per RECIST, CR was defined as disappearance of all target lesions, non-target lesions, and normalization of tumor marker level. PR was defined as greater than or equal to (≥)30 percent (%) decrease under baseline of the sum of the longest diameter (LD) of all target lesions. No unequivocal progression of non-target disease. No new lesions. Complete and partial responses must have been confirmed no less than 4 weeks after the criteria for response were first met.
Time Frame	Within 28 days of enrollment, Weeks 12 and 24
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	72
Percentage of Participants With Objective Clinical Response [units: percentage of participants] Number (95% Confidence Interval)	
CR+PR	88.9 (79.3 to 95.1)
CR+PR+NC	98.6 (92.5 to 99.9)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Breast-Conserving Surgery
Measure Description	Breast-conserving surgery was defined as lumpectomy + lymphadenectomy (LA), segmentectomy + LA, quadrantectomy + LA, or other (including sentinal node extirpation tumorectomy).
Time Frame	Week 24

Safety Issue?	No

Analysis Population Description

ITT population; only those participants who underwent surgery were included in the analysis

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	67
Percentage of Participants With Breast-Conserving Surgery [units: percentage of participants]	62.7

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Proliferation of Ki67
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. Biomarker Ki67 proliferation was defined as low (less than [<]15%) and high (≥15%).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Population evaluable for anatomopathological response with evaluable levels of the specified biomarker; data were missing for 2 participants.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	65
Percentage of Participants With pCR by Proliferation of Ki67 [units: percentage of participants]	
High proliferative index (n=50)	24.0
Low proliferative index (n=15)	13.3

Statistical Analysis 1 for Percentage of Participants With pCR by Proliferation of Ki67

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4915
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Kisspeptin (KISS1) Amplification
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. KISS1 amplification was defined as 1 (aneuploid), 2 (normal), 4 (amplification), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	23
Percentage of Participants With pCR by Kisspeptin (KISS1) Amplification [units: percentage of participants]	
Anueploid (n=8)	12.5
Normal (n=13)	30.77
Amplification (n=2)	50.0

Statistical Analysis 1 for Percentage of Participants With pCR by Kisspeptin (KISS1) Amplification

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4864
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by KISS1 Protein Expression

Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. KISS1 protein expression was defined as 0 (no expression), 1 (normal), 2 (augmented expression), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	25
Percentage of Participants With pCR by KISS1 Protein Expression [units: percentage of participants]	
No expression (n=18)	27.8
Normal (n=3)	66.7
Augmented expression (n=4)	50.0

Statistical Analysis 1 for Percentage of Participants With pCR by KISS1 Protein Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3613
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Vascular Endothelial Growth Factor Receptor (VEGFR) Amplification
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. VEFGR amplification was defined as 1 (aneuploid), 2 (normal), 4 (amplification), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	23
Percentage of Participants With pCR by Vascular Endothelial Growth Factor Receptor (VEGFR) Amplification [units: percentage of participants]	
Anueploid (n=1)	0
Normal (n=18)	33.3
Amplification (n=4)	0

Statistical Analysis 1 for Percentage of Participants With pCR by Vascular Endothelial Growth Factor Receptor (VEGFR) Amplification

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6605
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by VEGFR Protein Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. VEGFR protein expression was defined as 0 (no expression), 1 (normal), 2 (augmented expression), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	22

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Percentage of Participants With pCR by VEGFR Protein Expression [units: percentage of participants]	
No expression (n=7)	28.6
Normal (n=5)	40.0
Augmented expression (n=10)	20.0

Statistical Analysis 1 for Percentage of Participants With pCR by VEGFR Protein Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8311
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Hypoxia Inducible Factor (HIF) Protein Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. HIF protein expression was defined as 0 (no expression), 1 (normal), 2 (augmented expression), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	38
Percentage of Participants With pCR by Hypoxia Inducible Factor (HIF) Protein Expression [units: percentage of participants]	
No expression (n=25)	40.0
Normal (n=8)	12.5
Augmented expression (n=5)	60.0

Statistical Analysis 1 for Percentage of Participants With pCR by Hypoxia Inducible Factor (HIF) Protein Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.2230
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Endothelial Nitric Oxide Synthase (ENOS) Protein Expression

Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. ENOS protein expression was defined as 0 (no expression), 1 (normal), 2 (augmented expression), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	38
Percentage of Participants With pCR by Endothelial Nitric Oxide Synthase (ENOS) Protein Expression [units: percentage of participants]	
No expression (n=24)	29.2
Normal (n=10)	40.0
Augmented expression (n=4)	25.0

Statistical Analysis 1 for Percentage of Participants With pCR by Endothelial Nitric Oxide Synthase (ENOS) Protein Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8696
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Angiotension Protein Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. Angiotensin protein expression was defined as 0 (no expression), 1 (normal), 2 (augmented expression), or NE (not evaluated).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	26
Percentage of Participants With pCR by Angiotension Protein Expression [units: percentage of participants]	
No expression (n=14)	7.1
Normal (n=1)	0.0
Augmented expression (n=11)	63.6

Statistical Analysis 1 for Percentage of Participants With pCR by Angiotension Protein Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0074
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

12. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Vascular Endothelial Growth Factor (VEGF) Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. VEGF gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Percentage of Participants With pCR by Vascular Endothelial Growth Factor (VEGF) Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=1)	100.0
Gene expression below housekeeping level (n=33)	30.3

Statistical Analysis 1 for Percentage of Participants With pCR by Vascular Endothelial Growth Factor (VEGF) Gene Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3235
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

13. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by VEGFR Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. VEGFR gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by VEGFR Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=7)	0.0
Gene expression below housekeeping level (n=27)	40.7

Statistical Analysis 1 for Percentage of Participants With pCR by VEGFR Gene Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0693
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Phosphorylated AKT (pAKT) Gene Expression

Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. pAKT gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by Phosphorylated AKT (pAKT) Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=0)	NA [1]
Gene expression below housekeeping level (n=34)	32.4

[1] No participants assessed had PAKT gene expression above the housekeeping level.

15. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by HIF Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. HIF gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)

Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by HIF Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=9)	44.4
Gene expression below housekeeping level (n=25)	28.0

Statistical Analysis 1 for Percentage of Participants With pCR by HIF Gene Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4254
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

16. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Insulin-Like Growth Factor (IGF) Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. IGF gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by Insulin-Like Growth Factor (IGF) Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=0)	NA [1]
Gene expression below housekeeping level (n=34)	32.4

[1] All participants assessed had IGF gene expression levels below the housekeeping level.

17. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by ENOS Gene Expression

Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. ENOS gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by ENOS Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=1)	0
Gene expression below housekeeping level (n=33)	33.3

Statistical Analysis 1 for Percentage of Participants With pCR by ENOS Gene Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.0000
	Comments	[Not specified]

	Method	Fisher Exact
	Comments	[Not specified]

18. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Phosphorylated MAP Kinase (pMAPK) Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. pMAPK gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by Phosphorylated MAP Kinase (pMAPK) Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=30)	33.3
Gene expression equal to housekeeping level (n=1)	0
Gene expression below housekeeping level (n=3)	33.3

Statistical Analysis 1 for Percentage of Participants With pCR by Phosphorylated MAP Kinase (pMAPK) Gene Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.0000
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

19. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by Angiotensin II Receptor Type I (AGTR) Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. AGTR gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	33

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Percentage of Participants With pCR by Angiotensin II Receptor Type I (AGTR) Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=0)	NA [1]
Gene expression below housekeeping level (n=33)	30.3

[1] All participants had AGTR gene exptression below the housekeeping level.

20. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by KISS1 Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. KISS1 gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by KISS1 Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=1)	0.0

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Gene expression below housekeeping level (n=33)	33.3

Statistical Analysis 1 for Percentage of Participants With pCR by KISS1 Gene Expression

Statistical Analysis Overview	Comparison Groups	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	1.0000
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

21. Secondary Outcome Measure:

Measure Title	Percentage of Participants With pCR by RKISS1 Gene Expression
Measure Description	The percentage of participants with pCR was determined by anatomopathological study after completion of 8 cycles of study treatment. The anatomopathological study of the surgical piece was performed and assessed according to the Miller-Payne criteria. It was only considered pCR in the case of absence of invasive tumour cells in the breast and lymph nodes. RKISS1 gene expression was defined as below the housekeeping reference level (>0), above the housekeeping reference level (<0), or equal to the housekeeping reference level (0).
Time Frame	After Week 24 (surgery)
Safety Issue?	No

Analysis Population Description

Only those participants evaluated for the specified biomarker were included in the analysis.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Measured Values

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
Number of Participants Analyzed	34
Percentage of Participants With pCR by RKISS1 Gene Expression [units: percentage of participants]	
Gene expression above housekeeping level (n=0)	NA [1]
Gene expression below housekeeping level (n=34)	32.4

[1] All participants had RKISS1 gene expression below the housekeeping level.

Reported Adverse Events

Time Frame	Adverse events (AEs) were reported from the day of informed consent to the last date of contact for all participants.
Additional Description	All enrolled participants who received at least 1 dose of study treatment. This study did not include a separate analysis of non-serious AEs therefore non-serious adverse events presented in this record include all adverse events reported during the study, not just non-serious events.

Reporting Groups

	Description
Doxorubicin + Cyclophosphamide/ Bevacizumab + Docetaxel	Participants received doxorubicin 60 mg/m^2 IV followed by cyclophosphamide 600 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles. Participants then received bevacizumab 15 mg/kg IV followed by docetaxel 75 mg/m^2 IV on Day 1, repeated every 3 weeks for a maximum of 4 cycles.

Serious Adverse Events

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Affected/At Risk (%)
Total	13/72 (18.06%)
Blood and lymphatic system disorders	
Neutrophils/granulocytes [A] *	4/72 (5.56%)
Gastrointestinal disorders	

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Affected/At Risk (%)
Mucositis/stomatitis [A] *	2/72 (2.78%)
Vomiting [A] *	1/72 (1.39%)
Infections and infestations	
Febrile neutropaenia [B] *	6/72 (8.33%)
Infection with normal absolute neutrophil count (ANC) or grade 1 or 2 neutrophils [A] *	1/72 (1.39%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 13.0
B Term from vocabulary, NCI-CTCAE v 3.0

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Affected/At Risk (%)
Total	71/72 (98.61%)
Blood and lymphatic system disorders	
Hemoglobin [A] *	5/72 (6.94%)
Leukocytes (total WBC) [A] *	4/72 (5.56%)
Neutrophils/granulocytes [A] *	10/72 (13.89%)
Cardiac disorders	
Hypertension [A] *	7/72 (9.72%)
Endocrine disorders	
Hot flashes/flushes [A] *	5/72 (6.94%)
Eye disorders	
Watery eye (epiphora, tearing) [B] *	7/72 (9.72%)
Gastrointestinal disorders	

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Affected/At Risk (%)
Anorexia [A] *	5/72 (6.94%)
Constipation [A] *	14/72 (19.44%)
Diarrhoea [A] *	17/72 (23.61%)
Heartburn/dyspepsia [A] *	6/72 (8.33%)
Mucositis/stomatitis [B] *	43/72 (59.72%)
Nausea [A] *	43/72 (59.72%)
Taste alteration (dysgeusia) [A] *	6/72 (8.33%)
Vomiting [A] *	24/72 (33.33%)
General disorders	
Fatigue (asthenia, lethargy, malaise) [A] *	44/72 (61.11%)
Fever [A] *	14/72 (19.44%)
Flu-like syndrome [A] *	9/72 (12.5%)
Other - not specified [A] *	5/72 (6.94%)
Pain [A] *	36/72 (50%)
Immune system disorders	
Allergic reaction/hypersensitivity (including drug fever) [A] *	14/72 (19.44%)
Infections and infestations	
Febrile neutropaenia [A] *	4/72 (5.56%)
Infection with normal ANC or grade 1 or 2 neutrophils [B] *	17/72 (23.61%)
Metabolism and nutrition disorders	
ALT, SGPT (serum glutamic pyruvic transaminase) [B] *	4/72 (5.56%)

	Doxorubicin + Cyclophosphamide/Bevacizumab + Docetaxel
	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders	
Other - not specified [A] *	6/72 (8.33%)
Renal and urinary disorders	
Other - not specified [A] *	5/72 (6.94%)
Reproductive system and breast disorders	
Irregular menses (change from baseline) [A] *	11/72 (15.28%)
Respiratory, thoracic and mediastinal disorders	
Cough [B] *	4/72 (5.56%)
Hemorrhage, pulmonary/upper respiratory [A] *	12/72 (16.67%)
Skin and subcutaneous tissue disorders	
Hair loss/alopecia [A] *	36/72 (50%)
Nail changes [A] *	12/72 (16.67%)
Other - not specified [A] *	4/72 (5.56%)
Rash: hand-foot skin reaction [A] *	4/72 (5.56%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 13.0
B Term from vocabulary, NCI-CTCAE v 3.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:
Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request the Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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