Clinical trial results:
Phase II Study Evaluating the Efficacy and Tolerance of Bevacizumab (AVASTIN®) in HER2- Inflammatory Breast Cancer

Summary

EudraCT number	2008-001807-53
Trial protocol	FR
Global end of trial date	26 September 2019

Results information

Result version number	v1 (current)
This version publication date	05 November 2021
First version publication date	05 November 2021

Trial information

Trial identification

Sponsor protocol code	PACS 09 / 0802

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00820547
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75013
Public contact	Nourredine AIT-RAHMOUNE, UNICANCER, 33 1 71 93 67 04 , n.ait-rahmoune@unicancer.fr
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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	13 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the impact of concomitantly administering bevacizumab and neo-adjuvant chemotherapy, based on anthracyclines and taxanes, on the complete pathological response rate using mastectomy in patients with inflammatory breast cancer not overexpressing HER2.

Protection of trial subjects:

In order to ensure the protection of the rights, safety and well-being of trial subjects, this clinical trial was conducted in accordance with the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 January 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	8 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 100
Worldwide total number of subjects	100
EEA total number of subjects	100

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)	88

From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was national, multicentric phase II, open-label, non randomized, non controlled study, evaluating bevacizumab in the treatment of women ≥18 years old with HER2-negative inflammatory breast cancer. Patients were recruited in the study from 19-jan-2009 to 08-Sep-2010.

Pre-assignment

Screening details:

The study consisted of a screening phase of up to 30 days before treatment initiation to establish eligibility and document baseline measurements, a treatment phase (28-day treatment cycles; 52 weeks), a long-term follow-up to monitor progression-free survival, relapse-free survival, overall survival, and safety.

Period 1

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

Arms

Arm title	Bevacizumab

Arm description:

patients received 15 mg/kg bevacizumab every 3 weeks for 54 weeks (in 2 phases) or until disease progression, inacceptable toxicity, or patient refusal.

Arm type	Experimental
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Bevacizumab was administered at the dose of 15 mg/kg (IV infusion over 90 minutes [+/- 15 minutes] for the first administration and over 60 minutes [+/- 10 minutes] for the second administration if good tolerance, over 30 minutes [+/- 10 minutes] thereafter for the next administrations if good tolerance) every 3 weeks. Bevacizumab was administrated during 8 cycles in neoadjuvant treatment (concomitant of FEC100 then docetaxel before surgery) then 10 cycles in adjuvant cycles (concomitant of radiotherapy and hormonotherapy). The average treatment duration with bevacizumab was 54 weeks (18 injections).

Number of subjects in period 1	Bevacizumab
Started	100
Completed	100

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	100	100	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	88	88	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
median	49		
full range (min-max)	21 to 75	-	
Gender categorical Units: Subjects			
Female	100	100	
Male	0	0	
ECOG Units: Subjects			
ECOG 0	88	88	
ECOG 1	12	12	
Weight Units: kilogram(s)			
median	70		
full range (min-max)	45 to 117	-	
size Units: meter			
median	1.62		
full range (min-max)	1.45 to 1.84	-	

Subject analysis sets

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

Subject analysis set description:

All patients included in the study, whether or not they may have received one treatment dose.

Reporting group values	ITT population		
Number of subjects	100		
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)	88		
From 65-84 years	12		
85 years and over	0		
Age continuous Units: years			
median	49		
full range (min-max)	21 to 75		
Gender categorical Units: Subjects			
Female	100		
Male	0		
ECOG Units: Subjects			
ECOG 0	88		
ECOG 1	12		
Weight Units: kilogram(s)			
median	70		
full range (min-max)	45 to 117		
size Units: meter			
median	1.62		
full range (min-max)	1.45 to 1.84		

End points

End points reporting groups

Reporting group title	Bevacizumab

Reporting group description:

patients received 15 mg/kg bevacizumab every 3 weeks for 54 weeks (in 2 phases) or until disease progression, inacceptable toxicity, or patient refusal.

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

Subject analysis set description:

All patients included in the study, whether or not they may have received one treatment dose.

Primary: Complete pathological response

End point title	Complete pathological response[1]

End point description:

The primary endpoint was the complete pathological response on the operative specimen, after mastectomy, according to Sataloff criteria.

End point type	Primary

End point timeframe:

After mastectomy

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint was pathological complete response in breast and axillary lymph nodes after neoadjuvant treatment. The decision rule was that if fewer than 22 (22%) pathological complete responses were seen, the regimen would be regarded as insufficiently active.

End point values	Bevacizumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: percent				
number (confidence interval 95%)	19 (11.8 to 28.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival rate

End point title	Progression-free survival rate

End point description:

Progression-free survival at 3 and 5 years. Progression is defined as any local or regional relapse or any distant metastatic relapse, or any contralateral relapse, or any second cancer (except baso-cellular carcinoma, melanoma, in situ carcinoma of the cervix, in situ colon carcinoma, or in situ lobular carcinoma of the breast), or death of any cause.

End point type	Secondary

End point timeframe:

3 and 5 years

End point values	Bevacizumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: percent				
number (confidence interval 95%)				
3-year	56 (46 to 65)			
5-year	45 (35 to 55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free interval

End point title	Relapse-free interval

End point description:

The Relapse-free interval (RFI) at 3 and 5 years was calculated based on the date of patient inclusion until the date of relapse. Relapse is defined as any local, regional, or distant metastasis disease recurrence

End point type	Secondary

End point timeframe:

3 and 5 years

End point values	Bevacizumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: percent				
number (confidence interval 95%)				
3-year	98 (92 to 99)			
5-year	93 (84 to 97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival rate at 3 and 5 years. The time interval to death was calculated from the date of patient inclusion until the date of death

End point type	Secondary

End point timeframe:
3 and 5 years

End point values	Bevacizumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: percent				
number (confidence interval 95%)				
3-year	75 (66 to 83)			
5-year	59 (48 to 68)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall period of the study (up to 8 years after first study intake)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Bevacizumab

Reporting group description:

Patients received 15 mg/kg bevacizumab every 3 weeks for 54 weeks (in 2 phases) or until disease progression, inacceptable toxicity, or patient refusal.

Serious adverse events	Bevacizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 100 (51.00%)		
number of deaths (all causes)	25		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Liver metastases			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasm of uncertain behaviour of meninges			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombosis venous			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Catheter thrombosis			

subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis cerebral vein			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Abscess breast drainage			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abscess management			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise and Fatigue			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Wound healing delayed			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Wound healing disturbance of			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Drug hypersensitivity			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnea exacerbated			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory insufficiency			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Melancholia			

subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Colonoscopy			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Bone fracture (not spontaneous)			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin injury			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Wound surface unfolded			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular dysfunction			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Heart failure NYHA class IV			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile aplasia			
subjects affected / exposed	9 / 100 (9.00%)		
occurrences causally related to treatment / all	1 / 11		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	18 / 100 (18.00%)		
occurrences causally related to treatment / all	9 / 22		
deaths causally related to treatment / all	0 / 0		
Lymphocele			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anal ulcer			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Colitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mucositis oral				
subjects affected / exposed	7 / 100 (7.00%)			
occurrences causally related to treatment / all	5 / 7			
deaths causally related to treatment / all	0 / 0			
Tooth fracture				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Cellulitis staphylococcal				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Infection urinary tract				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Proteinuria				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Anal abscess				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
axillary abscess				

subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
infection urinary tract				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
local infection of skin and subcutaneous tissue, other				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
infection wound bacterial				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Potassium deficiency				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Bevacizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 100 (100.00%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	29 / 100 (29.00%)		
occurrences (all)	71		
Hypertension			
subjects affected / exposed	42 / 100 (42.00%)		
occurrences (all)	131		
Lymphocele			
subjects affected / exposed	12 / 100 (12.00%)		
occurrences (all)	20		
Surgical and medical procedures			
Radioepidermitis			
subjects affected / exposed	14 / 100 (14.00%)		
occurrences (all)	18		
General disorders and administration site conditions			
Wound healing			
subjects affected / exposed	24 / 100 (24.00%)		
occurrences (all)	39		
Asthenia			
subjects affected / exposed	100 / 100 (100.00%)		
occurrences (all)	401		
Fever			
subjects affected / exposed	67 / 100 (67.00%)		
occurrences (all)	87		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 100 (14.00%)		
occurrences (all)	20		
Dyspnoea			
subjects affected / exposed	16 / 100 (16.00%)		
occurrences (all)	24		
Rhinitis			

subjects affected / exposed occurrences (all)	36 / 100 (36.00%) 65		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 6 / 100 (6.00%) 16		
Investigations Abnormal liver function test subjects affected / exposed occurrences (all)	 18 / 100 (18.00%) 52		
Cardiac disorders Cardiovascular toxicity subjects affected / exposed occurrences (all)	 9 / 100 (9.00%) 13		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Peripheral neuropathy subjects affected / exposed occurrences (all)	 25 / 100 (25.00%) 59 53 / 100 (53.00%) 113 65 / 100 (65.00%) 137		
Blood and lymphatic system disorders Febrile neutropenia subjects affected / exposed occurrences (all) Anemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 36 / 100 (36.00%) 52 92 / 100 (92.00%) 329 98 / 100 (98.00%) 288 35 / 100 (35.00%) 50		

Eye disorders			
Conjunctivitis			
subjects affected / exposed	45 / 100 (45.00%)		
occurrences (all)	100		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	24 / 100 (24.00%)		
occurrences (all)	48		
Diarrhea			
subjects affected / exposed	43 / 100 (43.00%)		
occurrences (all)	59		
Dysphagia			
subjects affected / exposed	12 / 100 (12.00%)		
occurrences (all)	16		
Haemorrhoids			
subjects affected / exposed	23 / 100 (23.00%)		
occurrences (all)	37		
Mucositis			
subjects affected / exposed	100 / 100 (100.00%)		
occurrences (all)	352		
Nausea			
subjects affected / exposed	97 / 100 (97.00%)		
occurrences (all)	272		
Pyrosis			
subjects affected / exposed	9 / 100 (9.00%)		
occurrences (all)	10		
Xerostomia			
subjects affected / exposed	7 / 100 (7.00%)		
occurrences (all)	13		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	100 / 100 (100.00%)		
occurrences (all)	642		
Hand-foot syndrome			
subjects affected / exposed	11 / 100 (11.00%)		
occurrences (all)	15		

Nail toxicity			
subjects affected / exposed	32 / 100 (32.00%)		
occurrences (all)	67		
Skin toxicity			
subjects affected / exposed	93 / 100 (93.00%)		
occurrences (all)	182		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	59 / 100 (59.00%)		
occurrences (all)	159		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	100 / 100 (100.00%)		
occurrences (all)	277		
Infections and infestations			
Infection			
subjects affected / exposed	74 / 100 (74.00%)		
occurrences (all)	96		
Mycosis			
subjects affected / exposed	14 / 100 (14.00%)		
occurrences (all)	20		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	15 / 100 (15.00%)		
occurrences (all)	23		
Oedema			
subjects affected / exposed	23 / 100 (23.00%)		
occurrences (all)	29		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2008	In the first version of the protocol, post surgery bevacizumab was reintroduced concommittant with the radiotherapy. It was then decided to reintroduced bevacizumab at the same time of radiotherapy or at the latest during the week following the last radiotherapy session. Collection of a new blood sample was added before the initiation of cycle 5 to assess the correlation of CTC/CEC and proteomic with chemotherapy treatments (anthracycline and taxane).
29 March 2010	Modification of the procedure for the reporting of SAE grade 4 neutropenia without fever. A new paragraph was added to the protocol to specify that these particular SAE do not necessitate a declaration within the time delay specified by the article R.1123-47 of the Public Health Code. Due to their expected character they were reported to the Sponsor via toxicity report forms collected in the study CRF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported