



Clinical trial results:

A multicenter, randomised, open-label Phase II study to evaluate the clinical benefit of a post-operative treatment associating radiotherapy + Nivolumab + Ipilimumab versus radiotherapy + Capecitabine for triple negative breast cancer patients with residual disease after neoadjuvant chemotherapy.

Summary

EudraCT number	2017-003151-34
Trial protocol	FR
Global end of trial date	13 May 2024

Results information

Result version number	v1 (current)
This version publication date	30 October 2025
First version publication date	30 October 2025

Trial information

Trial identification

Sponsor protocol code	ET17-093
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Centre Léon Bérard
Sponsor organisation address	28 Rue Laënnec, Lyon, France,
Public contact	DRCI, Centre Léon Bérard, +33 426556824,
Scientific contact	DRCI, Centre Léon Bérard, +33 426556824,

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	12 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2024
Global end of trial reached?	Yes
Global end of trial date	13 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical benefit of a post-operative adjuvant therapy combining radiotherapy + Nivolumab + Ipilimumab versus radiotherapy + Capecitabine in in triple negative breast cancer (TNBC) patients with residual disease after neoadjuvant chemotherapy.

Protection of trial subjects:

Study treatments will continue to be administered as long as patient experiences clinical benefit in the opinion of the investigator or symptomatic deterioration attributed to disease progression as determined by the investigator after an integrated assessment of radiographic data and clinical status or withdrawal of consent.

The investigator will have to inform the patient of the study treatment, the objectives and the design of the study, as well as the biological samples collection, provide the patient information leaflet / Informed consent form, answer to any questions that the patient may have and ensure that she understands the potential risks and benefits of participating in the study before signing the informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 May 2019
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	France: 95
Worldwide total number of subjects	95
EEA total number of subjects	95

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)	95
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening period lasts for up to 28 days starting when the ICF is signed and ending before the first administration of study drugs (C1D1).

Period 1

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

Blinding implementation details:

last for up to 24 weeks (or at maximum 36 weeks in case of dose delay) starting at first study drugs intake and ending when the decision is made to permanently discontinue the study drugs.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Arm A
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Arm description:

Nivolumab (360 mg IV, every 3 weeks) for 8 doses and Ipilimumab (1 mg/kg, IV, every 6 weeks or every 2 doses of Nivolumab in case of dose delays) for 4 doses.

Arm type	Experimental
Investigational medicinal product name	OPDIVO®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Maximum of 8 doses Intravenous (IV).over a 24-week (or 36-week in case of dose delays) period or until disease recurrence, unacceptable toxicity, patient willingness to stop or withdrawal of consent

Investigational medicinal product name	Yervoy®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab (1 mg/kg, IV, every 6 weeks or every 2 doses of Nivolumab in case of dose delays) for 4 doses.

Arm title	Arm B
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Arm description:

Capecitabine (1000 mg/m² twice a day, Bis In Die [BID]), 14 days on / 7 days off for 8 cycles

Arm type	Standard treatment
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Capecitabine, oral, 1000 mg/m², twice a day for 14 days followed by a 7-day rest period.

Up to 8 cycles over a 24-week period (or 36-week in case of dose delays) or until disease recurrence, unacceptable toxicity, patient willingness to stop, or withdrawal of consent

Number of subjects in period 1	Arm A	Arm B
Started	45	50
Treatment period	-	-
Follow-up period	-	-
Completed	45	50

Baseline characteristics

Reporting groups

Reporting group title	Arm A
Reporting group description: Nivolumab (360 mg IV, every 3 weeks) for 8 doses and Ipilimumab (1 mg/kg, IV, every 6 weeks or every 2 doses of Nivolumab in case of dose delays) for 4 doses.	
Reporting group title	Arm B
Reporting group description: Capecitabine (1000 mg/m2 twice a day, Bis In Die [BID]), 14 days on / 7 days off for 8 cycles	

Reporting group values	Arm A	Arm B	Total
Number of subjects	45	50	95
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	45	50	95
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
median	47	46	
full range (min-max)	29 to 79	31 to 82	-
Gender categorical			
Units: Subjects			
Female	45	50	95
Male	0	0	0

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Nivolumab (360 mg IV, every 3 weeks) for 8 doses and Ipilimumab (1 mg/kg, IV, every 6 weeks or every 2 doses of Nivolumab in case of dose delays) for 4 doses.	
Reporting group title	Arm B
Reporting group description:	
Capecitabine (1000 mg/m2 twice a day, Bis In Die [BID]), 14 days on / 7 days off for 8 cycles	

Primary: Disease free survival

End point title	Disease free survival ^[1]
End point description:	
The primary endpoint is the Disease free survival. DFS is defined as the time from randomization until the date of the first relapse (local/regional recurrence or distant metastasis) or death (from any cause) whichever comes firsts and regardless of whether the patient withdraws from randomised study treatment or receives another anti-cancer therapy prior to disease relapse. Patients with no event at the time of the analysis will be censored at the date of the last adequate tumor assessment. It will be analysed based on the data from the ITT population. DFS will be estimated using the Kaplan-Meier method and will be described in terms of median and 2-year DFS per arm. Associated 2-sided 95% CI for the estimates will be provided. DFS distributions will be compared between the 2 study arms using a 2-sided Log-Rank test (significance level of 5%) stratified by centers, PS ECOG and RCB Class, supported by a stratified Cox regression. Hazard ratio will be provided its 95% CI.	
End point type	Primary
End point timeframe:	
DFS is defined as the time from randomization until the date of the first relapse (local/regional recurrence or distant metastasis) or death (from any cause)	
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: No difference was observed between the 2 arms (HR=0.84 ; CI95%=0.45-1.59 ; log-rank test pvalue =0.59).	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	50		
Units: Proportion				
number (confidence interval 95%)				
12 months	0.67 (0.51 to 0.78)	0.64 (0.49 to 0.76)		
36 months	0.62 (0.46 to 0.75)	0.60 (0.45 to 0.72)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

The investigator collects (spontaneous patient report or questioning) and immediately notifies the sponsor of all SAEs, in a written report, whether or not they are deemed to be attributable to research and which occur during the study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Grade 2 AEs were reported in 43 patients (96%) treated by NIVO+IPI vs 43 patients (86%) treated by Capecitabine and grade 3 AEs related to treatment were reported in 22 patients (49%) treated by NIVO+IPI vs 22 patients (44%) treated by Capecitabine. The most common Grade 2 AEs were Lymphocytes count decreased (43%), Radiation skin injury (28%), Fatigue (25%), Hyperthyroidism. AEs causing permanent treatment discontinuation occurred in 38% (17 pts) of NIVO+IPI vs 14% (7 pts) of Capecitabine.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 June 2019	Ancillary study on physical activity: addition of monthly monitoring for 6 months by a qualified teacher Updated list of investigators (Addition of 4 new centers and 25 investigators + Addition of two investigators in two already declared research locations) Resubmission of amendment to the CPP (06/08/2019) with the addition of details in the information note on the molecular analyses which will be carried out as part of the biological study associated with this trial, including gene analyses (expression and/or anomalies). These analyses were planned since the initial version of the protocol (Section 9.2) but not mentioned in the information note.
25 October 2019	Updated investigator brochure (Nivolumab requires specific monitoring and management of cardiac toxicities (myocarditis)). The risk of myocarditis was already mentioned in previous versions of the information notes. Updated investigator list (Change of principal investigator (PI) for the Paoli Calmette Institute center (Marseille) + Addition of 5 new centers and 24 investigators + Addition of an investigator for the Western Cancer Institute (Saint Herblain))
03 February 2020	Addition of a cortisol level measurement as recommended by the French Society of Endocrinology for patients undergoing immunotherapy Update of the list of investigators (declaration of 2 new centers and a new investigator in a research location already declared)
12 May 2020	Establishment of the additional monitoring committee after randomization and treatment for at least 1 cycle of the first 9 and 20 patients randomized in arm A. Update of the BI of ipilimumab Edition 23 of 03/11/2020 without impact on the protocol and transmission of the BI Edition 22 of 03/11/2019 for information purposes also without impact on the protocol. Request to resume the test after a temporary stop.
10 November 2020	Modification of inclusion criterion I6 to allow the inclusion of patients with residual disease of RCB class II (see justification below and in protocol V8.0 of 16/10/2020), consequently, modification of the hypotheses, the number and the duration of inclusions. Updating the list of investigators (Change of name and address of the Paul Strauss Centre + Addition of a center attached to the already declared participating center + Error found on an email address)
14 September 2021	Updating the list of investigators (declaration of a new participating center) The extension of the inclusion period by 12 months and consequently, of the total duration of the study. To date, 71 patients have been included out of the 114 planned.
09 November 2021	An urgent safety measure (USM) notification: Definitive cessation of inclusions with continuation of experimental treatments for patients still undergoing treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 October 2021	The definitive cessation of recruitment in the study	-

Notes:

Limitations and caveats

None reported