Clinical trial results:
A multicenter study to evaluate a risk-adapted strategy for treatment of extra cranial non seminomateous malignant germ cell tumour in children, adolescent and young adult

Summary

EudraCT number	2013-004039-60
Trial protocol	FR BE
Global end of trial date	14 October 2021

Results information

Result version number	v1 (current)
This version publication date	24 December 2025
First version publication date	24 December 2025

Trial information

Trial identification

Sponsor protocol code	ET13-016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02104986
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Léon Bérard
Sponsor organisation address	28 rue Laennec, Lyon, France, 69008
Public contact	Ellen BLANC, Centre Léon Bérard, +33 (0)4 78 78 28 28,
Scientific contact	Dr Cécile FAURE-CONTER , Centre Léon Bérard, +33 (0)4 78 78 28 28,

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	28 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2021
Global end of trial reached?	Yes
Global end of trial date	14 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the progression-free survival in patients with extra cranial non seminomateous malignant germ cell tumor (NSMGCT) and treated with chemiotherapy

Protection of trial subjects:

The investigator proceeded to the following information/procedures during the screening visit:
- Fully inform the patient of the study treatments, the objectives and the design of the study, answer to any questions that the patient may have and ensure that the patient understands the potential risks and benefits of participating in the study before signing the informed consent form. None study-related procedure can be started before ICF is signed and dated by both the patient (and impartial witness, if applicable).
- Check the eligibility criteria list and perform the exams

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 112
Worldwide total number of subjects	115
EEA total number of subjects	115

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)	25

Children (2-11 years)	23
Adolescents (12-17 years)	52
Adults (18-64 years)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at the time of enrolment at the participating sites. The declared investigator, after having identified a potential candidate for the study, informed her orally of the terms of the study and provide her with : an information note, An informed consent form that has been dated and signed by the patient and the investigator.

Pre-assignment

Screening details:

None study-related procedure can be started before ICF was signed and dated by both the patient (and impartial witness, if applicable) and the investigator - Checked the eligibility criteria list and perform the exams.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group IR1

Arm description:

Chemotherapy consists of 3 cycles of VBP (Vinblastine, Bleomycin, Cisplatin) and can be administered as an adjuvant to surgery or as neoadjuvant therapy.

Arm type	Experimental
Investigational medicinal product name	Vinblastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Vinblastine 3 mg/m²/j IVD at D1 + D2

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bleomycin 15 mg/m²/day IV 6 hours (UI = mg) at D1 + D2

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 33 mg/m²/day - IV 3 hours at D3 + D4 + D5

Arm title	Group IR2

Arm description:

Chemotherapy consists of 4 courses of VBP (Vinblastin, Bleomycin, Cisplatin) and can be administered as an adjuvant to surgery or as neoadjuvant therapy.

Arm type	Experimental

Investigational medicinal product name	Vinblastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

Vinblastine 3 mg/m²/day IVD at D1+ D2

Investigational medicinal product name	Bleomycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bleomycin 15 mg/m²/day IV 6 hours (UI = mg) at D1 + D2

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 33 mg/m²/day - IV 3 hours at D3 + D4 + D5

Arm title	Group HR1

Arm description:

Chemotherapy consists of 3 cycles of VIP (Vepedid/Etoposide, Ifosfamid, Cisplatin), (or BEP (Bleomycin, Etoposid, Cisplatin) if the patient is pubertal) and can be administered as an adjuvant to surgery or as a neoadjuvant.

Arm type	Experimental
Investigational medicinal product name	Vepesid
Investigational medicinal product code	
Other name	Etoposide
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Etoposide 75 mg/m²/day – IV 2 hours at D1 + D2 + D3 + D4 + D5

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ifosfamide 3 g/m²/day – IV 3 hours at D1 + D2

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 20 mg/m²/day - IV 3 hours at D1 + D2 + D3 + D4 + D5

Arm title	Group HR2

Arm description:

Chemotherapy consists of 4 cycles of VIP (Vepedid/Etoposide, Ifosfamid, Cisplatin), (or BEP (Bleomycin, Etoposid, Cisplatin) if the patient is pubertal) and can be administered as an adjuvant to surgery or as a neoadjuvant.

Arm type	Experimental
Investigational medicinal product name	Vepesid
Investigational medicinal product code	
Other name	Etoposide
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Etoposide 75 mg/m²/j – IV 2 heures at D1 + D2 + D3 + D4 + D5

Investigational medicinal product name	Ifosfamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ifosfamide 3 g/m²/day – IV 3 hours at D1 + D2

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 20 mg/m²/day - IV 3 hours at D1 + D2 + D3 + D4 + D5

Number of subjects in period 1	Group IR1	Group IR2	Group HR1
Started	20	11	30
Completed	20	11	30

Number of subjects in period 1	Group HR2
Started	54
Completed	54

Baseline characteristics

Reporting groups

Reporting group title	Overall period

Reporting group description:

No inclusion or exclusion criteria violation were recorded.
For 3 patients, treatment recommendations were not respected and these patients were excluded from the cohort. The final population analysis described in this report is 115 patients.

Reporting group values	Overall period	Total	
Number of subjects	115	115	
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)	26	26	
Children (2-11 years)	33	33	
Adolescents (12-17 years)	41	41	
Adults (18-64 years)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	12.8		
full range (min-max)	0.4 to 18.9	-	
Gender categorical Units: Subjects			
Female	68	68	
Male	47	47	

Subject analysis sets

Subject analysis set title	Overall period
Subject analysis set type	Intention-to-treat

Subject analysis set description:

No inclusion or exclusion criteria violation were recorded.
For 3 patients, treatment recommendations were not respected and these patients were excluded from the cohort. The final population analysis described in this report is 115 patients.

Reporting group values	Overall period		
Number of subjects	115		
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)	24		
Children (2-11 years)	23		
Adolescents (12-17 years)	53		
Adults (18-64 years)	15		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
median	12.8		
full range (min-max)	0.4 to 18.9		
Gender categorical			
Units: Subjects			
Female	68		
Male	47		

End points

End points reporting groups

Reporting group title	Group IR1

Reporting group description:

Chemotherapy consists of 3 cycles of VBP (Vinblastine, Bleomycin, Cisplatin) and can be administered as an adjuvant to surgery or as neoadjuvant therapy.

Reporting group title	Group IR2

Reporting group description:

Chemotherapy consists of 4 courses of VBP (Vinblastin, Bleomycin, Cisplatin) and can be administered as an adjuvant to surgery or as neoadjuvant therapy.

Reporting group title	Group HR1

Reporting group description:

Chemotherapy consists of 3 cycles of VIP (Vepedid/Etoposide, Ifosfamid, Cisplatin), (or BEP (Bleomycin, Etoposid, Cisplatin) if the patient is pubertal) and can be administered as an adjuvant to surgery or as a neoadjuvant.

Reporting group title	Group HR2

Reporting group description:

Chemotherapy consists of 4 cycles of VIP (Vepedid/Etoposide, Ifosfamid, Cisplatin), (or BEP (Bleomycin, Etoposid, Cisplatin) if the patient is pubertal) and can be administered as an adjuvant to surgery or as a neoadjuvant.

Subject analysis set title	Overall period
Subject analysis set type	Intention-to-treat

Subject analysis set description:

No inclusion or exclusion criteria violation were recorded.
For 3 patients, treatment recommendations were not respected and these patients were excluded from the cohort. The final population analysis described in this report is 115 patients.

Primary: Progression-free survival

End point title	Progression-free survival[1]

End point description:

End point type	Primary

End point timeframe:

2 years ≥ 80% despite a limit on the number of courses of treatment to 4 if a complete clinical and biological biological remission

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: After a median follow-up of 42.7 months (95% CI = 39–50.1) following the first cycle of chemotherapy, 11 patients progressed (9.6%) and 6 deaths (5.2%) were reported. The 2-year progression-free survival rate was 89% (95% CI = 81–93). As a reminder, the study objective was to observe a 2-year progression-free survival rate greater than 80%. The 2-year overall survival rate was 95% (95% CI = 89–98).

End point values	Overall period			
Subject group type	Subject analysis set			
Number of subjects analysed	115			
Units: 2 years ≥ 80%	115			

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 questionning) and immediately notifies the sponsor of all SAEs, in a written report, wether or not theay are deemed to be attributable to research and wich occur during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Frequency threshold for reporting non-serious adverse events: 1 %

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: The most frequently observed adverse events in the study were: decreased neutrophil count (20.9%), post-chemotherapy vomiting (12.2%), neutropenia (12.2%), and febrile aplasia (12.2%). Nineteen patients (16.5%) had abnormal hearing during follow-up, but 8 of them experienced hearing recovery.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2014	-Update the list of investigators. - Protocol modification (MNS)
22 September 2014	Update the list of investigators
17 February 2015	- Update the list of investigators ; - Inform of a reformulation of the definition of SAEs not requiring immediate reporting by the investigator.
20 September 2015	- Update the list of investigators ; - Change in RCP used as reference for safety information on bleomycin.
05 April 2016	Update the list of investigators ; Change RCP
12 December 2017	-Update the list of investigators. - Protocol modification (MNS)
27 March 2018	Update the list of investigators
13 November 2018	- Pharmacovigilance section updated; - Study documents brought into compliance with the General Data Protection Regulation (GDPR); - Investigator list updated:
09 July 2019	Update the list of the investigators
13 October 2021	- Reducing the follow-up time for patients from 5 years to a minimum of 2.5 years ; - Modification of the phase of the study (phase II instead of III) ; - Other non-substantial changes to the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported