Clinical trial results:
Diffuse large B cell non-hodgkin's lymphoma in the vulnerable/frail elderly. A multicentrix randomized phase II trial with emphasis on geritaric assesment and quality of life.

Summary

EudraCT number	2008-001506-16
Trial protocol	FR
Global end of trial date	20 December 2017

Results information

Result version number	v1 (current)
This version publication date	05 September 2025
First version publication date	05 September 2025

Trial information

Trial identification

Sponsor protocol code	IB 2005-33

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00911183
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Institut Bergonié
Sponsor organisation address	229 cours de l'Argonne, Bordeaux, France, 33076
Public contact	Regulatory Affairs Management Desk, Institut Bergonié, drci@bordeaux.unicancer.fr
Scientific contact	Regulatory Affairs Management Desk, Institut Bergonié, drci@bordeaux.unicancer.fr

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	27 September 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal objective of the trial is to assess the therapeutic efficacy (in terms of complete remission at 6 month, as defined by Cheson et al. 1999) and the safety of R-COP and R-COPY in vulnerable/frail elderly patients with diffuse large B cell non-Hodgkin's lymphoma.

Protection of trial subjects:

A supervisory committee is constitued to evaluate the benefit/risk ratio along the study period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 67
Worldwide total number of subjects	67
EEA total number of subjects	67

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)	0
From 65 to 84 years	55
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

Patients were included between Dec 2008 and June 2012.

Pre-assignment

Screening details:

INCLUSION CRITERIA
- Age 70 years and older.
- Diffuse large B cell lymphoma NHL CD20 positive according to the WHO classification including all morphological and clinical variants and excluding Burkitt-like lymphoma (presence of small cells in the bone marrow biopsy is allowed).
- Previously untreated
- Ann Arbor stages II-IV

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm I (R-COP regimen)

Arm description:

Patients receive rituximab IV, cyclophosphamide IV, and vincristine sulfate IV on day 1. Patients also receive oral prednisone on days 1-5 and filgrastim subcutaneously (SC) on days 8-14 or pegfilgrastim SC on day 2. Treatment repeats every 21 days for at least 3 courses.

Arm type	Experimental
Investigational medicinal product name	filgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

5 µg/kg, d8 to d14

Investigational medicinal product name	pegfilgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

5 µg/kg, d8 to d14

Investigational medicinal product name	rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m² on d1

Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

750 mg/m², d1

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

Dosage and administration details:

40 mg/m², d1 to d5

Investigational medicinal product name	vincristine sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1.4 mg/m², d1

Arm title	Arm II (R-COPY regimen)

Arm description:

Patients receive rituximab, cyclophosphamide, vincristine sulfate, prednisone, and filgrastim or pegfilgrastim as in arm I. Patients also receive liposome-encapsulated doxorubicin citrate IV on day 1. Treatment repeats every 21 days for at least 3 courses.

Arm type	Experimental
Investigational medicinal product name	filgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

5 µg/kg, d8 to d14

Investigational medicinal product name	pegfilgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

5 µg/kg, d8 to d14

Investigational medicinal product name	rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m², d1

Investigational medicinal product name	cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

750 mg/m², d1

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

Dosage and administration details:
40 mg/m², d1 to d5

Investigational medicinal product name	vincristine sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:
1.4 mg/m², d1 (max. : 2 mg)

Investigational medicinal product name	liposome-encapsulated doxorubicin citrate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:
40 mg/m², d1

Number of subjects in period 1	Arm I (R-COP regimen)	Arm II (R-COPY regimen)
Started	47	20
Completed	47	20

Baseline characteristics

Reporting groups	
Reporting group title	Arm I (R-COP regimen)
Reporting group description:	
Patients receive rituximab IV, cyclophosphamide IV, and vincristine sulfate IV on day 1. Patients also receive oral prednisone on days 1-5 and filgrastim subcutaneously (SC) on days 8-14 or pegfilgrastim SC on day 2. Treatment repeats every 21 days for at least 3 courses.	
Reporting group title	Arm II (R-COPY regimen)
Reporting group description:	
Patients receive rituximab, cyclophosphamide, vincristine sulfate, prednisone, and filgrastim or pegfilgrastim as in arm I. Patients also receive liposome-encapsulated doxorubicin citrate IV on day 1. Treatment repeats every 21 days for at least 3 courses.	

Reporting group values	Arm I (R-COP regimen)	Arm II (R-COPY regimen)	Total
Number of subjects	47	20	67
Age categorical Units: Subjects			
Age >= 70	47	20	67
Age continuous Units: years			
arithmetic mean	82.8	81.1	
standard deviation	± 4.2	± 4.1	-
Gender categorical Units: Subjects			
Female	24	10	34
Male	23	10	33

End points

End points reporting groups

Reporting group title	Arm I (R-COP regimen)

Reporting group description:

Patients receive rituximab IV, cyclophosphamide IV, and vincristine sulfate IV on day 1. Patients also receive oral prednisone on days 1-5 and filgrastim subcutaneously (SC) on days 8-14 or pegfilgrastim SC on day 2. Treatment repeats every 21 days for at least 3 courses.

Reporting group title	Arm II (R-COPY regimen)

Reporting group description:

Patients receive rituximab, cyclophosphamide, vincristine sulfate, prednisone, and filgrastim or pegfilgrastim as in arm I. Patients also receive liposome-encapsulated doxorubicin citrate IV on day 1. Treatment repeats every 21 days for at least 3 courses.

Primary: Number of subjects in Complete Remission 6 Months After Randomization

End point title	Number of subjects in Complete Remission 6 Months After Randomization[1]

End point description:

Complete remission [CR] is defined according to Cheson criteria. CR requires the following:
1. Complete disappearance of all detectable clinical and radiographic evidence of disease and disappearance of all disease-related symptoms if present before therapy, and normalization of those biochemical abnormalities.
2. All lymph nodes and nodal masses must have regressed to normal size. Previously involved nodes that were 1.1 to 1.5 cm in their greatest transverse diameter before treatment must have decreased to ≤1 cm in their greatest transverse diameter after treatment, or by more than 75% in the sum of the products of the greatest diameters (SPD).
3. The spleen, if considered to be enlarged before therapy on the basis of a CT scan, must have regressed in size and must not be palpable on physical examination.
4. If the bone marrow was involved by lymphoma before treatment, the infiltrate must be cleared on repeat bone marrow aspirate and biopsy of the same site.

End point type	Primary

End point timeframe:

6 Months After Randomization

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 statistical analysis was performed. This not a comparative trial. The complete remission rates were reported for each population (no comparison performed).

End point values	Arm I (R-COP regimen)	Arm II (R-COPY regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	20		
Units: subjects	14	9		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with severe toxicity 6 Months After Randomization

End point title	Number of subjects with severe toxicity 6 Months After Randomization[2]

End point description:

Sevevre toxicity is defined as the occurrence of severe toxicity, that is, febrile neutropenia, or toxic death, within one month following the end of the treatment.
Febrile neutropenia is defined in the International CTC toxicity scale as “fever of unknown origin without clinically or microbiologically documented infection: neutrophils < 1.0 x 109/l and fever ≥38.5° C”.
Toxic death is defined as any death which occur during treatment (from day 1 of the first cycle of chemotherapy up to day 30 of the last cycle) and is not related to lymphoma. Yet, because of the peculiarity of the patients treated (vulnerable/frail), because of previous experience of the occurrence of such death neither related to toxicity nor to lymphoma (EORTC 20992 phase II trial), interpretation of each death cause will be evaluated by

End point type	Primary

End point timeframe:

6 Months After Randomization

Notes:

[2] - 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 statistical analysis was performed. This not a comparative trial. The toxicity rates were reported for each population (no comparison performed).

End point values	Arm I (R-COP regimen)	Arm II (R-COPY regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	20		
Units: subjects	10	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS is defined as the delay between the date of randomization and the date of death

End point type	Secondary

End point timeframe:

from randomization, up to 5 years

End point values	Arm I (R-COP regimen)	Arm II (R-COPY regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	20		
Units: months				
median (confidence interval 95%)	20.1 (10.4 to 25.4)	25.4 (12.2 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free suvival (PFS)

End point title	Progression-free suvival (PFS)

End point description:

Delay between the date of randomization and the date of progression or death. Progression is defined according to the Cheson criteria.

End point type	Secondary

End point timeframe:

from randomization, up to 5 years

End point values	Arm I (R-COP regimen)	Arm II (R-COPY regimen)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	20		
Units: months				
median (confidence interval 95%)	10.4 (5.4 to 25.9)	18.0 (5.2 to 999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Non-serious adverse events were not collected.
Serious adverse events were reported from the signature of the informed consent form to 30 days after the study end participation of the patient.

Adverse event reporting additional description:

Non-serious adverse events were not collected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11

Reporting groups

Reporting group title	Arm I (R-COP Regimen)
Reporting group description: -	
Reporting group title	Arm II (R-COPY Regimen)
Reporting group description: -	

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: non serious adverse events were not collected

Serious adverse events	Arm I (R-COP Regimen)	Arm II (R-COPY Regimen)	
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 47 (97.87%)	20 / 20 (100.00%)	
number of deaths (all causes)	27	12	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphomateous meningitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Venous thrombosis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory insufficiency			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatoid bronchitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Distress respiratory			
subjects affected / exposed	4 / 47 (8.51%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Dyspnea			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial pneumonitis			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis allergic			

subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 47 (2.13%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
femure fracture			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrythmia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aurticular fibrillation			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiogenic shock			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarct			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Accident cerebrovascular			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
convulsion			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Febrile aplasia			
subjects affected / exposed	4 / 47 (8.51%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 47 (6.38%)	2 / 20 (10.00%)	
occurrences causally related to treatment / all	4 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dysphagia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			

subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sigmoiditis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pseudomonas			
subjects affected / exposed	0 / 47 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	5 / 47 (10.64%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	3 / 5	1 / 1	
deaths causally related to treatment / all	2 / 3	1 / 1	
sepsis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
virosis			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Hematuria			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clotridium difficile colitis			
subjects affected / exposed	2 / 47 (4.26%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter septicemia			
subjects affected / exposed	0 / 47 (0.00%)	2 / 20 (10.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
dehydratation			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperuricemia			
subjects affected / exposed	1 / 47 (2.13%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm I (R-COP Regimen)	Arm II (R-COPY Regimen)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 47 (0.00%)	0 / 20 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 May 2008	Protocol V2 dated 15-apr-2008
27 August 2008	Protocol V3 dated 06-aug-2008
24 June 2009	Protocol v4 dated 26-mar-2009
28 April 2010	Protocol V5 dated 26-mar-2010
15 December 2010	Protocol V6 dated 27-sep-2010

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported