



Clinical trial results: EuroNet-Paediatric Hodgkin's Lymphoma Group Second International Inter-Group Study for Classical Hodgkin's Lymphoma in Children and Adolescents

Summary

EudraCT number	2012-004053-88
Trial protocol	DE BE AT CZ ES IT NL DK FR PL FI GB SE NO
Global end of trial date	31 October 2024

Results information

Result version number	v1 (current)
This version publication date	12 December 2025
First version publication date	12 December 2025
Summary attachment (see zip file)	Synopsis ICH E3 (EuroNet-PHL-C2_Summary_of_Trial_report_Final1.0_2025-10-21.pdf)

Trial information

Trial identification

Sponsor protocol code	EuroNet-PHL-C2
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Amendment 7 international: Amendment 7 international

Notes:

Sponsors

Sponsor organisation name	Justus-Liebig-University
Sponsor organisation address	Rudolf-Buchheim-Str. 23, Giessen-Marburg, Germany, 35392
Public contact	Zentrum für Kinderheilkunde, Justus Liebig University of Giessen, +49 641 9854342, dieter.koerholz@paediat.med.uni-giessen.de
Scientific contact	Zentrum für Kinderheilkunde, Justus Liebig University of Giessen, +49 641 9854342, dieter.koerholz@paediat.med.uni-giessen.de

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	21 October 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

3.4.1.1 Randomised

1. To increase event-free survival in ERA(early response assessment) PET-negative intermediate and advanced stage patients (TL-2 and TL-3) without radiotherapy by using intensified consolidation chemotherapy (DECOPDAC-21).

2. To demonstrate in ERA PET-positive TL-2 and TL-3 patients that the combination of intensified consolidation chemotherapy (DECOPDAC-21) plus restricted field RT to sites that remain FDG-PET positive at the late response assessment (LRA) is comparable to the standard consolidation chemotherapy (COPDAC-28) plus standard involved node radiotherapy.

3.4.1.2 Non-randomised

3. To further reduce the radiotherapy indication in early stage patients by increasing the threshold for a positive FDG PET scan at early response assessment (ERA) to Deauville 4+ while still preserving a 5 year EFS estimate at a target of 90% or above.

Protection of trial subjects:

Patients were closely monitored by the treatment team with regard to safety.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
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	Australia: 127
Country: Number of subjects enrolled	New Zealand: 34
Country: Number of subjects enrolled	Norway: 37
Country: Number of subjects enrolled	Czechia: 65
Country: Number of subjects enrolled	Israel: 151
Country: Number of subjects enrolled	Switzerland: 51
Country: Number of subjects enrolled	Netherlands: 124
Country: Number of subjects enrolled	Poland: 112
Country: Number of subjects enrolled	Spain: 155

Country: Number of subjects enrolled	Sweden: 24
Country: Number of subjects enrolled	United Kingdom: 169
Country: Number of subjects enrolled	Austria: 90
Country: Number of subjects enrolled	Belgium: 111
Country: Number of subjects enrolled	Denmark: 21
Country: Number of subjects enrolled	France: 332
Country: Number of subjects enrolled	Germany: 715
Country: Number of subjects enrolled	Italy: 556
Worldwide total number of subjects	2874
EEA total number of subjects	2342

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)	573
Adolescents (12-17 years)	2165
Adults (18-64 years)	136
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Within this clinical trial 2921 patients were recruited in 17 participating countries with 239 active trial sites.

Date of first enrolment: 2015-10-01

Date of last completed: 2024-10-31

Pre-assignment

Screening details:

Confirmation of the diagnosis by local pathologist and national reference pathologist; physical examination; medical history; laboratory analyses; imaging (PET); previous and concomitant disease status; fertility consideration; ECG

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	TL-1

Arm description:

stage IA/IB/IIA with ESR < 30 and without bulk.

Two cycles of OEPA followed by early response assessment (ERA) including FDG-PET.

Patients in TL-1 with a negative ERA PET scan are consolidated with one additional cycle of COPDAC-28.

Patients in TL-1 with a positive PET scan at ERA will receive involved node radiotherapy to all initially involved sites.

Arm type	Standard for minor infestation
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5 mg/m² i.v., capping dose 2 mg
day 1 + 8 + 15

Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg/m²/day p.o. divided into 3 doses
day 1 – 15

Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/m² per 1-6 hour infusion
day 1 + 15

Investigational medicinal product name	Etoposide/Etopophos
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

125 mg/m² Etoposide (NB: 142 mg Etoposide phosphate equals 125 mg etoposide); 2hrs infusion time day 1 – 5

Arm title	TL2+3 Rando AR
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Arm description:

This arm includes patients who show an adequate response at ERA. After initial staging and assignment to treatment level 2 or 3 patients have been randomised between DECOPDAC-21 or COPDAC-28.

Patients assigned to TL-2 receive two cycles, patients assigned to TL-3 receive four cycles consolidation treatment according to the respective randomisation result.

Arm type	Experimental
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5 mg/m² i.v., capping dose 2 mg day 1 + 8 + 15

Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg/m²/day p.o. divided into 3 doses day 1 – 15

Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 mg/m² per 1-6 hour infusion day 1 + 15

Investigational medicinal product name	Etoposide/Etopophos
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

125 mg/m² Etoposide (NB: 142 mg Etoposide phosphate equals 125 mg etoposide); 2hrs infusion time day 1 – 5

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5 mg/m² i.v., capping dose 2 mg

day 1 + 8

Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

40 mg/m²/day p.o. divided into 3 doses

day 1 – 8, no capping dose

Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

25 mg/m² per 1-6 hour infusion

day 1

Investigational medicinal product name	Etoposide/Etopophos
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

125 mg/m² Etoposide (NB: 142 mg Etoposide phosphate equals 125 mg etoposide); 2hrs infusion time
day 1 – 5

Investigational medicinal product name	Dacarbazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

250 mg/m² per 15 – 30 min. infusion

day 1 – 3

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

625 mg/m², 60-min. infusion

day 1 and day 2

optional: concomitant intravenous hydration with glucose/saline solution at a rate of 3 l/m² over 24 hours

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.5 mg/m² i.v., capping dose 2 mg

day 1 + 8

Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 40 mg/m ² /day p.o. divided into 3 doses day 1 – 8, no capping dose	
Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 25 mg/m ² per 1-6 hour infusion day 1	
Investigational medicinal product name	Etoposide/Etopophos
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 125 mg/m ² Etoposide (NB: 142 mg Etoposide phosphate equals 125 mg etoposide); 2hrs infusion time day 1 – 5	
Investigational medicinal product name	Dacarbazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion
Dosage and administration details: 250 mg/m ² per 15 – 30 min. infusion day 1 – 3	
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 625 mg/m ² , 60-min. infusion day 1 and day 2 optional: concomitant intravenous hydration with glucose/saline solution at a rate of 3 l/m ² over 24 hours	
Arm title	TL2+3 Rando IR
Arm description: This arm includes patients who show an insufficient response at ERA. After initial staging and assignment to treatment level 2 or 3 patients have been randomised between DECOPDAC-21 or COPDAC-28. Patients assigned to TL-2 receive two cycles, patients assigned to TL-3 receive four cycles consolidation treatment according to the respective randomisation result. These patients with a positive PET scan at ERA (IR) subsequently underwent additional radiotherapy.	
Arm type	Experimental
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use
Dosage and administration details: 1.5 mg/m ² i.v., capping dose 2 mg day 1 + 8 + 15	

Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 60 mg/m ² /day p.o. divided into 3 doses day 1 – 15	
Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 40 mg/m ² per 1-6 hour infusion day 1 + 15	
Investigational medicinal product name	Etoposide/Etopophos
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 125 mg/m ² Etoposide (NB: 142 mg Etoposide phosphate equals 125 mg etoposide); 2hrs infusion time day 1 – 5	
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use
Dosage and administration details: 1.5 mg/m ² i.v., capping dose 2 mg day 1 + 8	
Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 40 mg/m ² /day p.o. divided into 3 doses day 1 – 8, no capping dose	
Investigational medicinal product name	Doxorubicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: 25 mg/m ² per 1-6 hour infusion day 1	
Investigational medicinal product name	Etoposide/Etopophos
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

125 mg/m² Etoposide (NB: 142 mg Etoposide phosphate equals 125 mg etoposide); 2hrs infusion time
day 1 – 5

Investigational medicinal product name	Dacarbazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

250 mg/m² per 15 – 30 min. infusion
day 1 – 3

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

625 mg/m², 60-min. infusion
day 1 and day 2

optional: concomitant intravenous hydration with glucose/saline solution at a rate of 3 l/m² over 24 hours

Number of subjects in period 1^[1]	TL-1	TL2+3 Rando AR	TL2+3 Rando IR
Started	444	1442	802
Completed	442	1442	802
Not completed	2	0	0
Consent withdrawn by subject	1	-	-
Physician decision	1	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: See uploaded Trial Report (*.pdf)

End points

End points reporting groups

Reporting group title	TL-1
Reporting group description: stage IA/IB/IIA with ESR < 30 and without bulk. Two cycles of OEPA followed by early response assessment (ERA) including FDG-PET. Patients in TL-1 with a negative ERA PET scan are consolidated with one additional cycle of COPDAC-28. Patients in TL-1 with a positive PET scan at ERA will receive involved node radiotherapy to all initially involved sites.	
Reporting group title	TL2+3 Rando AR
Reporting group description: This arm includes patients who show an adequate response at ERA. After initial staging and assignment to treatment level 2 or 3 patients have been randomised between DECOPDAC-21 or COPDAC-28. Patients assigned to TL-2 receive two cycles, patients assigned to TL-3 receive four cycles consolidation treatment according to the respective randomisation result.	
Reporting group title	TL2+3 Rando IR
Reporting group description: This arm includes patients who show an insufficient response at ERA. After initial staging and assignment to treatment level 2 or 3 patients have been randomised between DECOPDAC-21 or COPDAC-28. Patients assigned to TL-2 receive two cycles, patients assigned to TL-3 receive four cycles consolidation treatment according to the respective randomisation result. These patients with a positive PET scan at ERA (IR) subsequently underwent additional radiotherapy.	

Primary: EFS

End point title	EFS ^[1]
End point description: Event-free survival (EFS) defined as time from start of treatment until the first of the following events: o progression/relapse of disease o secondary malignancy o death from any cause	
End point type	Primary
End point timeframe: 60 months	
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: See uploaded Trial Report (*pdf)	

End point values	TL-1	TL2+3 Rando AR	TL2+3 Rando IR	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	422	1338	678	
Units: whole	422	1338	678	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

The observation period for adverse events begins at start of treatment and is restricted to events occurring within 3 months after the end of the trial treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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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: See uploaded Trial Report (*pdf)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 July 2015	<p>Since the Coordinating investigator moved from Halle to another university (Justus Liebig University, Gießen) the Sponsor of the trial has changed. In addition, the study office will be located in Giessen from November 2015 on. Thus, all essential documents have to be changed.</p> <p>Also, one of the inclusion criteria regarding the upper limit of age in countries Australia and New Zealand has been adjusted. This change has been considered for the update of the synopsis to trial protocol, too.</p>
01 June 2016	<p>For all participating countries</p> <p>A) Relocation of Reference Centre from the University Hospital Halle to University Gießen/Marburg and study centre from Martin-Luther University Halle to Justus Liebig University Gießen; and clarification in PIC.</p> <p>B) Local contacts of the respective treating hospitals should be visualized on the letterhead of the PIC docs as long as country specific regulations allow this.</p> <p>C) Clarification in the protocol that the study group no longer differentiates between upper, middle and lower mediastinum, but only between upper and lower mediastinum.</p> <p>D) Clarification in the protocol that for Follow-up MRI i.v. contrast is not necessary.</p> <p>E) Clarification that in addition to photon radiotherapy also radiotherapy with protons may be used for radiotherapy of residual lymphoma in selected cases using the same dose and fractioning concepts and overall radiotherapy treatment time. (Only if country specific regulations consider the use of protons as standard of care as long as dose and fractioning dose do not differ from photon treatment.)</p> <p>F) Description in detail the process to organize quality control of radiotherapy within the appendix IV of the protocol.</p> <p>For Germany only</p> <p>A) Changes in two already approved country-specific side projects.</p> <p>B) Two new country-specific scientific side projects in Germany will be initiated.</p> <p>C) The study committee of the GPOH Hodgkin lymphoma study group elected Prof. Gattenlöhner as the newly acting coordinating reference pathologist in Germany.</p>

15 May 2017	<p>A)Change of DMC members B)Change of reference pathologist Norway C)Listing of Israeli reference pathologist D)Clarification on the term adverse reaction E)Correction of typing errors and wrong English wording, replacement of abbreviated Rt doses by actual RT doses throughout the text F)Correction of RT dose. The standard RT dose (protocol vs. flow diagram) G)Correction of orientation of figure 14 and 15 H)Clarification on adequate contraception incl. correction in PIC docs I)Clarification on Regulations for Trial drug in Non-EU States J)Clarification on randomisation procedure and process K)Clarification regarding screening and pre-treatment investigations that are mandatory and those that are recommendations. L)Recognition of the different country specific requirements for parents providing consent for minors and use of full names. M)Clarification on indication for bone scan N)Implementation of guidance regarding vomiting after oral prednisone O)Clarification on frequency of recalculation body surface area P)Clarification on dose management in obese patients Q)Clarification that mesna in DECOPDAC may be used according to local guidelines incl. splitting the cyclophosphamide dose into two days R)Clarification on ECG if anthracycline dose exceeds 200 mg/m² in DECOPDAC S)Clarification of the different RT strategies for E-lesion and disseminated organ involvement T)Clarification of: Patient Withdrawal, Exclusion, Termination of individual trial treatment, Lost to follow-up U)Updated RT-Manual V)Clarification on exceptions from expedited SAE reporting W)Clarification regarding different national requirements for investigators X)Harmonisation of statements in protocol and monitoring Manual Y)Revision to sections III.1, III.2, III.3 and III.4 – to clarify which investigations are mandatory or recommendations Z)Clarification on imaging at suspected relapse AA)Clarification on maximum concentration of etoposide in solution</p>
31 July 2017	<p>1.1. Shifting the threshold for a negative LRA-PET (= end-of-treatment PET) from qPET 0.95 to qPET 1.3. 1.2. Documentation of patient data from pregnant partners of a trial subject or pregnant trial subjects and their newborns 1.3. Consideration of new information on Prednisolone in the patient information and the trial protocol 1.4. Update of patient information for country-specific side projects in Germany with respect to storage of blood samples. 1.5. Addition country-specific side projects (Italy and Netherlands), which may be open to other countries, if the necessary regulatory processes are fulfilled in the respective countries 1.6. Update of exceptions from expedited SAE reporting 1.7. Update of reference radiology in the central review board 1.8. Increasing the quality standard for reference pathology in Germany (accreditation according to DIN ISO 17020)</p>
01 August 2019	<p>1.1. Opening of the side project B-3 all EuroNet-PHL countries which are willing to participate in this project 1.2. Opening of the side project G "Gonadal function and fertility" in all EuroNet-PHL countries which are willing to participate in this project 1.3. Opening of the side project I "Immunodeficiency in Hodgkin Lymphoma" in all EuroNet-PHL countries which are willing to participate in this project 1.4. Opening of the Country-specific side project "Circulating cell-free DNA in classical Hodgkin Lymphoma in children adolescents and Young adults. The HOLY study." 1.5. Detailed description of radiotherapy quality control 1.6. Implementation of the new data protection regulations in the German informed consent forms as well as in the English template for international use, if applicable in the respective country 1.7. Update of administrative data (contact data etc.)</p>

05 September 2020	1.1. Early stop of patient registration 1.2. The final analysis will take place as soon as the median follow-up is 60 months (current internationally standard) and if 85% of the patients at least have reached 36 months follow-up at least. 1.3. Update of administrative data (contact data etc.)
04 July 2024	1.1. Earlier last patient last visit date 1.2. Final analysis planned for first quarter of 2025 1.1. Update of administrative data (contact data etc.)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported