Clinical trial results:
BIO-CHIC-Study
BIOmarker driven and dose intensified CHemoImmunotherapy with early CNS prophylaxis in patients less than 65 years with high risk diffuse large B-cell lymphoma

Summary

EudraCT number	2015-002846-30
Trial protocol	FI DK NO SE
Global end of trial date	30 January 2025

Results information

Result version number	v1 (current)
This version publication date	06 June 2026
First version publication date	06 June 2026
Summary attachment (see zip file)	BIO-CHIC results summary (BIO-CHIC results summary.pdf)

Trial information

Trial identification

Sponsor protocol code	NLG-LBC-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01325194
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	HUS , Comprehensive Cancer Center
Sponsor organisation address	Haartmaninkatu 4, Helsinki, Finland, 00290
Public contact	Sirpa Leppä, HUH Comprehensive Cancer Centre, 358 504270820, sirpa.leppa@hus.fi
Scientific contact	Sirpa Leppä, HUH Comprehensive Cancer Centre, 358 504270820, sirpa.leppa@hus.fi

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	30 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Failure free survival rate (FFS) of the patients with biological risk factors compared to similar patients from the historical CRY-04 and CHIC studies, with spesific focus on three years survival.

Protection of trial subjects:

Supportive care:
Medication to prevent nausea
G-CSF to reduce neutropenia and to reduce the risk of neutropenic infection
Pneumocystis prophylaxis
Blood transfusions in case of gr 3 anemia and gr 4 trombocytopenia

Background therapy:

As listed above

Evidence for comparator:

No comparator

Actual start date of recruitment	03 October 2016
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	Norway: 35
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Denmark: 34
Country: Number of subjects enrolled	Finland: 55
Worldwide total number of subjects	127
EEA total number of subjects	127

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)	127
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment started in 6.6.2017 and ended 2.2.2021

Pre-assignment

Screening details:

127 patients were included. 4 were not eligible due to unsuccessful stratification, resulting 123 patient intend-to-treat population.

Period 1

Period 1 title	Prephase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All patients

Arm description: -

Arm type	all
Investigational medicinal product name	Prednison
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100mg 3-6 days

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

Dosage and administration details:

1mg x1

Number of subjects in period 1	All patients
Started	127
Completed	127

Period 2

Period 2 title	Treatment
Is this the baseline period?	Yes[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Biologically high risk group, GROUP B

Arm description:

Patients with at least one of the following factor
- o Myc translocation (FISH)
- o Myc/Bcl2 double hits (FISH)
- o P53 deletion (FISH)
- o Myc+ and Bcl2+ (IHC; double expressors, DE)
- o P53+ (ICH)
- o CD5+ (IHC)

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

Dosage and administration details:

Continuous infusion for 96 h, 1,6mg/ m2, 6 cycles

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

Dosage and administration details:

375mg/m2, 7 cycles

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

Dosage and administration details:

750mg m2, 6 cycles

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

Dosage and administration details:

continuous infusion for 96h, 40mg/m2, 6 cycles

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

Dosage and administration details:

Continuous infusion for 96 h, 200mg/ m2, 4 cycles

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Intravenous use

Dosage and administration details:

3g/m2 in two cycles

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

Dosage and administration details:

12g/m2 one cycle

Arm title	Biologically low risk group, GROUP A

Arm description:

- o Myc translocation (FISH)
- o Myc/Bcl2 double hits (FISH)
- o P53 deletion (FISH)
- o Myc+ and Bcl2+ (IHC; double expressors, DE)
- o P53+ (ICH)
- o CD5+ (IHC)

Patients without the above listed factors

Arm type	Active comparator
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

375mg/ m2on D1 for 4 cycles

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

Dosage and administration details:

750mg/m2 for 4 cycles

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

Dosage and administration details:

50mg/m2 for 4 cycles

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

Dosage and administration details:

1.4mg/m2 on D1 for 4 cycles

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

Dosage and administration details:

100mg/m2 on Days 1-3 for 4 cycles

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

Dosage and administration details:

100mg for 5 days, for 4 cycles

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 is not a treatment period. Period 2 is the treatment period.

Number of subjects in period 2[2][3]	Biologically high risk group, GROUP B	Biologically low risk group, GROUP A
Started	61	62
Completed	56	57
Not completed	5	5
Consent withdrawn by subject	1	1
Adverse event, non-fatal	2	2
Lymphoma progression	2	2

Notes:

[2] - 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: Screening failures: 4 patients

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Stratification failure in 4 patients, in addition 6 patients (3 in high risk group, 3in low risk groups) discontinued the study due to AE or refractory disease.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment
Reporting group description:	
High risk and low risk groups	

Reporting group values	Treatment	Total	
Number of subjects	123	123	
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)	123	123	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	53	53	
Male	70	70	

End points

End points reporting groups

Reporting group title	All patients

Reporting group description: -

Reporting group title	Biologically high risk group, GROUP B

Reporting group description:

Patients with at least one of the following factor
- o Myc translocation (FISH)
- o Myc/Bcl2 double hits (FISH)
- o P53 deletion (FISH)
- o Myc+ and Bcl2+ (IHC; double expressors, DE)
- o P53+ (ICH)
- o CD5+ (IHC)

Reporting group title	Biologically low risk group, GROUP A

Reporting group description:

- o Myc translocation (FISH)
- o Myc/Bcl2 double hits (FISH)
- o P53 deletion (FISH)
- o Myc+ and Bcl2+ (IHC; double expressors, DE)
- o P53+ (ICH)
- o CD5+ (IHC)

Patients without the above listed factors

Primary: Time to treatment failure

End point title	Time to treatment failure

End point description:

Interval between the registration date and the date of documented progression or lack of response, first relapse, death for any reason or discontinuation/change of therapy because of toxicity, whichever occurs first. Secondary hematologic malignancies (leukemia and MDS) are included as events in this category. Otherwise, patients will be censored at the last date they were known to be alive. For patients not responding at any time point on study treatment, TTF is defined as one day.

End point type	Primary

End point timeframe:

Interval between the registration date and the date of documented progression or lack of response, first relapse, death for any reason or discontinuation/change of therapy because of toxicity, whichever occurs first.

End point values	Biologically high risk group, GROUP B	Biologically low risk group, GROUP A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: % at 3 years	61	62		

Statistical analyses

Statistical analysis title	Kaplan-Meier and log rank
Comparison groups	Biologically high risk group, GROUP B v Biologically low risk group, GROUP A
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	> 0.3
Method	Logrank

Notes:

[1] - Different risk groups (no purpose to compare these)

Secondary: Progression free survival

End point title	Progression free survival

End point description:

The time from the registration date to the date of progression or death from any cause

End point type	Secondary

End point timeframe:

The time from the registration date to the date of progression or death from any cause

End point values	Biologically high risk group, GROUP B	Biologically low risk group, GROUP A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: % at 3 years	61	62		

Statistical analyses

Statistical analysis title	Kaplan-Meier and log rank
Comparison groups	Biologically low risk group, GROUP A v Biologically high risk group, GROUP B
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.27
Method	Logrank

Notes:

[2] - Different risk groups (no purpose to compare)

Secondary: Overall survival (all causes of death)

End point title	Overall survival (all causes of death)

End point description:

The time from the registration date to the date of death. Patients still alive or lost to follow-up are censored at the last date they were known to be alive.

End point type	Secondary

End point timeframe:

The time from the registration date to the date of death. Patients still alive or lost to follow-up are censored at the last date they were known to be alive.

End point values	Biologically high risk group, GROUP B	Biologically low risk group, GROUP A		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: % at 3 years	61	62		

Statistical analyses

Statistical analysis title	Kaplan-Meier and log rank
Comparison groups	Biologically high risk group, GROUP B v Biologically low risk group, GROUP A
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.51
Method	Logrank

Notes:

[3] - Different risk groups (no purpose to compare)

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
All adverse events occurring during the treatment period and within one month after the last treatment administration will be documented in the applicable eCRF section.	
Adverse event reporting additional description:	
Total of 143 SAEs were reported during the study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	NCI CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	Infection gradus 4
Reporting group description:	
Infection gradus 4	
Reporting group title	Renal gradus 3
Reporting group description: -	
Reporting group title	Gastrointestinal gradus 4
Reporting group description:	
Both low and high risk patients.	

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: Protocol only requested to record AEs higher than gr 2.

Serious adverse events	Infection gradus 4	Renal gradus 3	Gastrointestinal gradus 4
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 123 (1.63%)	3 / 123 (2.44%)	3 / 123 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infection			
subjects affected / exposed	2 / 123 (1.63%)	3 / 123 (2.44%)	3 / 123 (2.44%)
occurrences causally related to treatment / all	2 / 2	3 / 3	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Infection gradus 4	Renal gradus 3	Gastrointestinal gradus 4
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 123 (0.00%)	0 / 123 (0.00%)	0 / 123 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2017	• Primary End point was defined as PTTF (time to treatment failure) instead of FFS:n (failure free survival). • High riski group definition was amended to include Myc+ and/ or BCL2+ • Exclusion criteria list was refined • Monitoring Plan was included in the protocol (Appendix 8) • Contact details updated • Due to a delay in the start of the study, the enrollment period has been extended
14 March 2017	PO etoposide is allowed in cycles 4-6 on D2 and D3 as a part of CHOEP regimen
27 October 2017	Only minor changes and updates added.
18 April 2018	This amendment was made solely to comply with the requirements of the Swedish authorities. -A signature page has been added to the protocol - The administrative procedure has been clarified · The process of ICF has been clarified
14 June 2019	-Contact information of CTU has been updated -Recruitment time has been extended to 31.12.2020 - Use of rituximab biosimilars is allowed -Vincristine can be given on day -4 (+/- 3 days) during prophase -Plasma samples will be collected to STECK tubes. -GDPR rules concerning subjects rights have been included to the patient information form. -PI in Roskilde has changed -Contact information of the PI in Tampere has been corrected Oulu site has been closed Typos have been corrected

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported