



## Clinical trial results:

### A randomised evaluation of molecular guided therapy for diffuse large B-cell lymphoma with Bortezomib

#### Summary

EudraCT number	2010-022422-32
Trial protocol	GB
Global end of trial date	31 August 2021

#### Results information

Result version number	v1 (current)
This version publication date	24 May 2025
First version publication date	24 May 2025
Summary attachment (see zip file)	Primary results (1-s2.0-S1470204518309355-main.pdf) Final results (JCO 2023 - REMoDL-B Final results.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	RHMCAN0749
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##### Additional study identifiers

ISRCTN number	ISRCTN51837425
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	University Hospital Southampton NHS Foundation Trust
Sponsor organisation address	University Road, Highfield, Southampton, United Kingdom, SO17 1BJ
Public contact	Louise Stanton, University Hospital Southampton NHS Foundation Trust, l.stanton@soton.ac.uk
Scientific contact	Louise Stanton, University Hospital Southampton NHS Foundation Trust, l.stanton@soton.ac.uk

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:

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**Results analysis stage**

Analysis stage	Final
Date of interim/final analysis	30 June 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2015
Global end of trial reached?	Yes
Global end of trial date	31 August 2021
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

The primary objective of this trial is to demonstrate the effectiveness of bortezomib in combination with rituximab and CHOP chemotherapy (RB-CHOP) in comparison R-CHOP alone for the treatment of previously untreated patients with diffuse large B cell lymphoma. Efficacy will be determined by the number of patients who are alive and their condition has not progressed (Progression Free Survival). The study also will assess if the molecular profile (phenotype) (either ABC or GCB) determines the benefit from the addition of bortezomib.

Protection of trial subjects:

none

Background therapy:

none

Evidence for comparator: -

Actual start date of recruitment	02 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	United Kingdom: 1076
Worldwide total number of subjects	1076
EEA total number of subjects	0

Notes:

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**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)	546
From 65 to 84 years	528

85 years and over	2
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## Subject disposition

### Recruitment

Recruitment details:

Between June 2, 2011, and June 10, 2015, 1128 eligible patients were registered, of whom 918 (81%) were randomly assigned to receive treatment.

### Pre-assignment

Screening details:

Some patients with lymphoma with poor prognostic features at the presentation need to be excluded from such trials on the grounds of performance status or the need for urgent treatment before screening procedures can be completed.

### 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
<b>Arm title</b>	R-CHOP

Arm description:

All study patients will receive 1 cycle of conventional R-CHOP chemotherapy on a standard 21 day schedule.

Arm type	Active comparator
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Day 1

375mg/m<sup>2</sup>

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

Dosage and administration details:

Day 1

750mg/m<sup>2</sup>

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

Dosage and administration details:

Day 1

50mg/m<sup>2</sup>

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Day 1	
1.4mg/m2 (max 2mg)	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Day 1-5	
100mg, once a day	
<b>Arm title</b>	RB-CHOP
Arm description:	
Patients in this arm will receive 5 cycles of R-CHOP with bortezomib according to the schedule below	
Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Day 1	
375mg/m2	
Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Day 1 and Day 8	
1.6 mg/m2	
Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Day 1	
750mg/m2	
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Day 1	
50mg/m2	
Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion

Routes of administration	Intravenous use
Dosage and administration details:	
Day 1	
1.4mg/m <sup>2</sup> (max 2mg)	
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Day 1-5

100mg, once a day

<b>Number of subjects in period 1</b>	R-CHOP	RB-CHOP
Started	617	459
Completed	585	421
Not completed	32	38
withdraw before treatment	20	15
Lost to follow-up	12	23

## Baseline characteristics

### Reporting groups

Reporting group title	R-CHOP
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Reporting group description:

All study patients will receive 1 cycle of conventional R-CHOP chemotherapy on a standard 21 day schedule.

Reporting group title	RB-CHOP
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Reporting group description:

Patients in this arm will receive 5 cycles of R-CHOP with bortezomib according to the schedule below

Reporting group values	R-CHOP	RB-CHOP	Total
Number of subjects	617	459	1076
Age categorical			
Units: Subjects			
Adults (18-64 years)	291	255	546
From 65-84 years	324	204	528
85 years and over	2	0	2
Age continuous			
Units: years			
median	65	63	
full range (min-max)	24 to 86	20 to 84	-
Gender categorical			
Units: Subjects			
Female	274	206	480
Male	343	253	596
Bone marrow involvement			
Units: Subjects			
YES	112	63	175
NO	505	396	901
Molecular phenotype			
Units: Subjects			
Activated B cell	121	123	244
Germinal centre B cell	240	235	475
Unclassified	98	101	199
Unknown	158	0	158

## End points

### End points reporting groups

Reporting group title	R-CHOP
Reporting group description: All study patients will receive 1 cycle of conventional R-CHOP chemotherapy on a standard 21 day schedule.	
Reporting group title	RB-CHOP
Reporting group description: Patients in this arm will receive 5 cycles of R-CHOP with bortezomib according to the schedule below	

### Primary: progression-free survival events

End point title	progression-free survival events
End point description:	
End point type	Primary
End point timeframe: 30 months	

End point values	R-CHOP	RB-CHOP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	361	358		
Units: subjects	107	91		

### Statistical analyses

<b>Statistical analysis title</b>	30-month progression-free survival
Comparison groups	R-CHOP v RB-CHOP
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Kaplan-Meier estimate

<b>Statistical analysis title</b>	progression- free survival combined activation
Statistical analysis description: progression-free survival in the combined activated and germinal center B-cell populations	
Comparison groups	R-CHOP v RB-CHOP

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23
Method	Kaplan-Meier estimate

<b>Statistical analysis title</b>	progression-free survival in mITT population
Statistical analysis description:	
30-month progression-free survival in the mITT population	
Comparison groups	R-CHOP v RB-CHOP
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16
Method	Kaplan-Meier estimate

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

The reporting requirement for SAEs and AEs affecting patients applies for all events occurring up to 30 days after the last administration of study drugs. For details of adverse events see the attached PDF results papers.

Adverse event reporting additional description:

All unresolved adverse events should be followed by the investigator until resolved, the patient is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each patient to report any subsequent event(s) that the patient believes might related.

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Assessment type	Systematic
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### Dictionary used

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Dictionary name	Free text AEs & SAEs
Dictionary version	N/A

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Frequency threshold for reporting non-serious adverse events: 0 %

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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: There are no detailed adverse events provided as these were not coded to MEDRA but categorised based on free text. For details of the adverse and serious events experienced by patients in the study please see the PubMed web links and associated appendices and the attached PDFs. For details of all other endpoints too also see the attached PDF and web links.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2011	Protocol version 2, 11 sites added
20 April 2011	Protocol version 3 - Updates to Patient Information Sheet, Informed Consent Form and Protocol
06 September 2011	Protocol version 3 - Removal of named suppliers for study medication so local suppliers can be used
10 April 2012	Protocol version 4 - Changes to study drug labels
24 May 2012	Protocol version 5 - Addition of sites in Switzerland and updated Investigational Brochure for Bortezomib
13 May 2013	Protocol version 6 - PIS and ICF updated to include information about data being used for research purposes
28 March 2014	Protocol version 7 - Dosage regimen/duration of treatment Bortezomib now being given sub cutaneous and at an increased dose of 1.6mg/ m <sup>2</sup> ; Schedule of observations and procedures. Sites must have results for Hep B prior to registration and 12 lead ECG should be performed on all patients; PET/CT hybrid scanners may be used if scanner is of diagnostic quality and includes the use of IV contrast; Justification of switch from IV to SC for administration of Bortezomib statement; clarifications on various sections of the protocol
02 October 2014	Protocol version 8 - Sample size increased to 1,132
07 April 2016	Protocol version 9 - Update of IB (Ed 18). Clarification of analysis timepoints. Addition of a table, which holds all relevant IB and SmPC versions. Notification of sites to be closed: Queen Elizabeth Hospital Gateshead (Dr S Marshall) and Mid Staffordshire (Dr P Revell).
17 January 2019	Protocol version 10 - Clarification on analysis time points and updated SmPCs, PIS & ICF v.7 - data storage clarification now Rave on US server.
17 August 2021	Protocol version 11 - Change EOT definition to remove long term observational follow up - including new protocol.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None
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Notes:

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## Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30948276>

<http://www.ncbi.nlm.nih.gov/pubmed/36972491>