Clinical trial results:
Phase II, randomised, multicentre study with two treatment arms (R-COMP versus R-CHOP) in newly diagnosed elderly patients (?60 years) with non-localised diffuse large B-cell lymphoma (DLBCL)/follicular lymphoma grade IIIb.

Summary

EudraCT number	2013-001065-17
Trial protocol	ES
Global end of trial date	17 February 2016

Results information

Result version number	v1 (current)
This version publication date	02 July 2021
First version publication date	02 July 2021

Trial information

Trial identification

Sponsor protocol code	GEL-R-COMP-2013

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02012088
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GELTAMO
Sponsor organisation address	AVENIDA VALDECILLA, SANTANDER, Spain,
Public contact	GELTAMO, Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea, 0034 913195780, dm@geltamo.com
Scientific contact	GELTAMO, Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea, 0034 913195780, sc@geltamo.com

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	17 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

?To assess reduced of subclinical cardiotoxicity, determined by differences in LVEF, which involves the incorporation of non-pegylated liposomal doxorubicin (Myocet®) when replacing conventional doxorubicin in the standard R-CHOP regimen (R-COMP) to treat newly diagnosed elderly patients with non-localised DLBCL/follicular lymohoma grade IIIb

Protection of trial subjects:

Several strategies have been proposed to decrease cardiotoxicity provoked by anthracyclines in elderly populations.
These include the administration of reduced doses or slow infusions of doxorubicin, use of cardioprotective agents or substitution by other antineoplastic agents or by other less cardiotoxic anthacyclines, such as mitoxantrone, epirubicin, or liposomal formulations of doxorubicin.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2013
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	Spain: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	45
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The requirements for the patients to be included were: age 60 years, newly diagnosed non-localized DLBCL or grade 3b FL (those with localized lymphoma were included in the presence of bulky disease)

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	90
Number of subjects completed	90

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	R-CHOP arm

Arm description:

to receive R-CHOP (rituximab 375 mg/m2 [day 1], cyclophosphamide 750 mg/m2 [day 1], doxorubicin 50 mg/m2 [day 1], vincristine 1.4 mg/m2 [day 1, capped at a maximum of 2 mg], and prednisone 60mg/m2 [days 1–5]

Arm type	Experimental
Investigational medicinal product name	R-CHOP doxorubicin vincristine cyclophosphamid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were randomized 1:1 to receive R-CHOP (rituximab 375 mg/m2 [day 1], cyclophosphamide 750 mg/m2 [day 1], doxorubicin 50 mg/m2 [day 1], vincristine 1.4 mg/m2 [day 1, capped at a maximum of 2 mg], and prednisone 60mg/m2 [days 1–5]) o

Arm title	R-COMP arm

Arm description:

R-COMP (with the same drugs except for conventional

doxorubicin being replaced by non-pegylated liposomal doxorubicin, Myocet®, at doses of 50 mg/m2 [day 1in both arms every 21 days for a total of six cycles

Arm type	Experimental
Investigational medicinal product name	R-COMP Myocet®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

R-COMP (with the same drugs used in R-chop except for conventional doxorubicin being replaced by non-pegylated liposomal doxorubicin, Myocet®, at doses of 50 mg/m2 [day 1])

Number of subjects in period 1	R-CHOP arm	R-COMP arm
Started	45	45
Completed	45	45

Baseline characteristics

Reporting groups

Reporting group title	OVERALL TRIAL

Reporting group description: -

Reporting group values	OVERALL TRIAL	Total	
Number of subjects	90	90	
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)	0	0	
From 65-84 years	90	90	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	49	49	
Male	41	41	

Subject analysis sets

Subject analysis set title	All
Subject analysis set type	Full analysis

Subject analysis set description:

a clinical trial for patients 60 years old diagnosed with DLBCL or grade 3b follicular lymphoma (FL) with normal cardiac function, with the main objective of evaluating the possible benefits in terms of cardiac toxicity, of the substitution of conventional doxorubicin by non-pegylated liposomal doxorubicin (Myocet®, R-COMP arm) as part of R-CHOP therap

Reporting group values	All		
Number of subjects	90		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over	90		

Gender categorical Units: Subjects			
Female	49		
Male	41		

End points

End points reporting groups

Reporting group title	R-CHOP arm

Reporting group description:

to receive R-CHOP (rituximab
375 mg/m2
[day 1], cyclophosphamide 750 mg/m2
[day 1],
doxorubicin 50 mg/m2
[day 1], vincristine 1.4 mg/m2
[day 1,
capped at a maximum of 2 mg], and prednisone 60mg/m2
[days
1–5]

Reporting group title	R-COMP arm

Reporting group description:

R-COMP (with the same drugs except for conventional
doxorubicin being replaced by non-pegylated liposomal doxorubicin, Myocet®, at doses of 50 mg/m2
[day 1in both arms every 21 days for a total of six cycles

Subject analysis set title	All
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a clinical trial for patients 60 years old diagnosed with DLBCL
or grade 3b follicular lymphoma (FL) with normal cardiac
function, with the main objective of evaluating the possible
benefits in terms of cardiac toxicity, of the substitution of
conventional doxorubicin by non-pegylated liposomal doxorubicin (Myocet®, R-COMP arm) as part of R-CHOP therap

Primary: Primary

End point title	Primary

End point description:

The primary end point of the study was to evaluate the differences
in subclinical cardiotoxicity, defined by a decrease in LVEF to
<55% at the end of treatment (measured by echocardiography
at 1 month after therapy), in patients receiving the standard
R-CHOP regimen compared with those treated with R-COMP

End point type	Primary

End point timeframe:

Subclinical cardiac toxicity determined by the percentage of measurings experiencing a decrease in LEVF determined by echocardiography with final LEVF <55% 30 and/or 120 days after the end of the study treatment

End point values	R-CHOP arm	R-COMP arm	All	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	45	45	45	
Units: <55% 30	45	45	45	

Statistical analyses

Statistical analysis title	Complete analisis
Comparison groups	R-CHOP arm v R-COMP arm
Number of subjects included in analysis	90
Analysis specification	Post-hoc
Analysis type	other
P-value	< 5
Method	No imputation method

Secondary: Secondary

End point title	Secondary

End point description:

Secondary end points were efficacy in terms of overall
and complete response rates (ORR and CR) in all randomized
patients, event-free survival (EFS), progression-free survival
(PFS), overall survival (OS), and safety. Response to treatment was evaluated according to clinical, laboratory results
and the evaluation of imaging techniques according to the
criteria defined by Cheson et al.2

End point type	Secondary

End point timeframe:

30 and 120 days after the end of the study treatment

End point values	R-CHOP arm	R-COMP arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	45		
Units: ORR and CR	45	45		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

assessment of adverse events (AE) using version 4.0 of the NCI-CTCAE scale for grading toxicity, as well as the variations in cardiac biomarkers troponin and NTproBNP in both arms throughout the study

Assessment type	Non-systematic

Dictionary used

Dictionary name	NCI-CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Non-hematologic toxicity

Reporting group description: -

Serious adverse events	Non-hematologic toxicity		
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 90 (31.11%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	16 / 90 (17.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	12 / 90 (13.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Non-hematologic toxicity		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 90 (91.11%)		
Vascular disorders			

Anaemia subjects affected / exposed occurrences (all)	36 / 90 (40.00%) 1		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	46 / 90 (51.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported