Clinical trial results:
Allogeneic Transplantation of Haematopoietic Stem Cells Following Non-myeloablative Conditioning With Melphalan, Fludarabine, Thiotepa, Rituximab and Ibritumomab Tiuxetan (Zevalin) in Patients With Aggressive Non-Hodgkin's B-cell Lymphoma

Summary

EudraCT number	2007-003302-10
Trial protocol	ES
Global end of trial date	04 February 2013

Results information

Result version number	v1 (current)
This version publication date	15 July 2021
First version publication date	15 July 2021
Summary attachment (see zip file)	Z-RIC (ZRIC_30abril2015_corregidoLola_MC.pdf)

Trial information

Trial identification

Sponsor protocol code	GELTAMO- Z-RIC - Allo

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00644371
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GELTAMO
Sponsor organisation address	H. MARQUES DE VALDECILLA SERVICIO DE HEMATOLOGIA, SANTANDER, Spain, 39008
Public contact	GELTAMO, Grupo Español de Linfomas y Transplante Autólogo de Médula Ósea, 0034 913195780, dm@geltamo.com
Scientific contact	GELTAMO, Grupo Español de Linfomas y Transplante 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	04 February 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2011
Global end of trial reached?	Yes
Global end of trial date	04 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Progression-free survival

Protection of trial subjects:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study. Inclusion criteria were: achieving less than a partial response (PR) after 2 lines of treatment, relapse after autologous stem cell transplantation, positive PET after autologous stem cell transplantation or stem cell mobilization failure. Patients were eligible if they were between 18 and 65 years old, ECOG performance status was ≤2 and no major organ dysfunction was present (serum bilirubin < 2 mg/dL with AST, ALT, GGT and AP < 2 times ULN, left ventricular ejection fraction > 40% and serum creatinine < 2 mg/dL). Exclusion criteria included prior RIT, HIV associated lymphoma, pregnancy or breast feeding, severe comorbidities or known allergy to murine antibodies or Y-90.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2007
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: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	18

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study.
Patients were eligible if they were between 18 and 65 years old, ECOG performance status was ≤2

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	18
Number of subjects completed	18

Period 1

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

Arms

Arm title	Experimental

Arm description:

Experimental arm

Arm type	Experimental
Investigational medicinal product name	Ibritumomab Tiuxetan (Zevalin)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

0.4 mCi/kg (14.8 MBq/kg). Maximum: 32 mCi on day -14.

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

Dosage and administration details:

250 mg/m2 on days -21 and -14 and 0.4 mCi/kg of Y-90-IB was administered after rituximab dose

Investigational medicinal product name	Fludarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

30 mg/m2/day on days -7, -6, -5, -4 and -3 as a 30-min infusion.

Investigational medicinal product name	Melphalan
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

70 mg/m2/day on days -3 and -2 as a 15-min infusion.

Investigational medicinal product name	Thiotepa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg over 4 hours every 12 hours on day -8.

Number of subjects in period 1	Experimental
Started	18
Completed	18

Baseline characteristics

Reporting groups

Reporting group title	OVERALL TRIAL

Reporting group description: -

Reporting group values	OVERALL TRIAL	Total	
Number of subjects	18	18	
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)	18	18	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	15	15	

Subject analysis sets

Subject analysis set title	Overall trial
Subject analysis set type	Full analysis

Subject analysis set description:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study. Inclusion criteria were: achieving less than a partial response (PR) after 2 lines of treatment, relapse after autologous stem cell transplantation, positive PET after autologous stem cell transplantation or stem cell mobilization failure. Patients were eligible if they were between 18 and 65 years old, ECOG performance status was ≤2 and no major organ dysfunction was present (serum bilirubin < 2 mg/dL with AST, ALT, GGT and AP < 2 times ULN, left ventricular ejection fraction > 40% and serum creatinine < 2 mg/dL). Exclusion criteria included prior RIT, HIV associated lymphoma, pregnancy or breast feeding, severe comorbidities or known allergy to murine antibodies or Y-90.

Reporting group values	Overall trial		
Number of subjects	18		
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	18		
Gender categorical Units: Subjects			
Female	3		
Male	15		

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description: Experimental arm	
Subject analysis set title	Overall trial
Subject analysis set type	Full analysis

Subject analysis set description:

Patients with diagnosis of CD20 positive NHL, including diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL) or grade 3b or transformed follicular lymphoma (FL) were considered for the study. Inclusion criteria were: achieving less than a partial response (PR) after 2 lines of treatment, relapse after autologous stem cell transplantation, positive PET after autologous stem cell transplantation or stem cell mobilization failure. Patients were eligible if they were between 18 and 65 years old, ECOG performance status was ≤2 and no major organ dysfunction was present (serum bilirubin < 2 mg/dL with AST, ALT, GGT and AP < 2 times ULN, left ventricular ejection fraction > 40% and serum creatinine < 2 mg/dL). Exclusion criteria included prior RIT, HIV associated lymphoma, pregnancy or breast feeding, severe comorbidities or known allergy to murine antibodies or Y-90.

Primary: Primary

End point title	Primary
End point description: Progression-free survival	
End point type	Primary
End point timeframe: 12-months	

End point values	Experimental	Overall trial		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	18	18		
Units: pfs	18	18		

Statistical analyses

Statistical analysis title	Progression free survival
Comparison groups	Experimental v Overall trial
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 50
Method	Logrank
Parameter estimate	TTP

Notes:

[1] - PFS

Secondary: Secondary

End point title	Secondary

End point description:

safety (toxicity, transplantation- and graft-related mortality)
response to treatment according to the Cheson's criteria (Cheson B, et al. JCO 25, 570, 2007).
overall survival
relapse rate
acute and chronic Graft-versus-Host Disease
haematological and immunological reconstitution, and chimerism.
the impact of Complete Clinical Response, determined by flow cytometry and PET, on progression-free survival

End point type	Secondary

End point timeframe:

36 months

End point values	Experimental			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: pfs	18			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: On 4-year estimated PFS	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	3.0
Reporting groups	
Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 18 (38.89%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Septic shock			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 18 (16.67%)		
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	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 18 (61.11%)		
Blood and lymphatic system disorders			
Infection			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	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