Clinical trial results:
AN OPEN MULTICENTER PHASE II STUDY OF EFFICACY AND TOXICITY OF MAINTENANCE SUBCUTANEOUS RITUXIMAB AFTER RESCUE TREATMENT IN PATIENTS WITH RELAPSED OR REFRACTORY MANTLE-CELL LYMPHOMA NON-ELIGIBLE FOR AUTO OR ALLO STEM CELL TRANSPLANTATION.

Summary

EudraCT number	2014-001911-38
Trial protocol	ES
Global end of trial date	14 August 2019

Results information

Result version number	v1
This version publication date	12 June 2021
First version publication date	12 June 2021

Trial information

Trial identification

Sponsor protocol code	GELTAMOMAN2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02267915
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 TRASPLANTES AUTOLOGO DE MEDULA OSEA (GELTAMO), 0034 913195780, sc@geltamo.com
Scientific contact	GELTAMO, GRUPO ESPAÑOL DE LINFOMAS Y TRASPLANTES AUTOLOGO DE MEDULA OSEA (GELTAMO), 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	14 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2019
Global end of trial reached?	Yes
Global end of trial date	14 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Time to relapse/progression (TTP) after achieving a complete or partial response with the (R-GemOxD)-induction therapy

Protection of trial subjects:

Data base has been anonimated

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2014
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: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	4
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment
Recruitment details: -

Pre-assignment
Screening details: -

Pre-assignment period milestones	
Number of subjects started	19
Number of subjects completed	19

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: subcutaneous rituximab

Arm description:

Experimental: subcutaneous rituximab
MabThera 1400 mg solution for subcutaneous injection

Arm type	Experimental
Investigational medicinal product name	MABThera
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1400 mg

Number of subjects in period 1	Experimental: subcutaneous rituximab
Started	19
Completed	19

Baseline characteristics

Reporting groups

Reporting group title	OVERALL TRIAL

Reporting group description: -

Reporting group values	OVERALL TRIAL	Total	
Number of subjects	19	19	
Age categorical Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	13	13	
Gender categorical Units: Subjects			
Female	16	16	
Male	3	3	

Subject analysis sets

Subject analysis set title	All
Subject analysis set type	Full analysis

Subject analysis set description:

Time to relapse/progression (TTP) after achieving a complete or partial response with the (R-GemOxD)-induction
therapy

Reporting group values	All		
Number of subjects	19		
Age categorical Units: Subjects			
Adults (18-64 years)	6		
From 65-84 years	13		
Gender categorical Units: Subjects			
Female	16		
Male	3		

End points

End points reporting groups

Reporting group title	Experimental: subcutaneous rituximab

Reporting group description:

Experimental: subcutaneous rituximab
MabThera 1400 mg solution for subcutaneous injection

Subject analysis set title	All
Subject analysis set type	Full analysis

Subject analysis set description:

Time to relapse/progression (TTP) after achieving a complete or partial response with the (R-GemOxD)-induction
therapy

Primary: Primary

End point title	Primary

End point description:

This is a phase II trial evaluating the role of maintenance with subcutaneous Rituximab in patients with stage II-IV relapsed or
refractory mantle-cell lymphoma with complete or partial response after the administration of a salvage regimen with R-GemOxD.
Before the study start and in order to standardize the results, the same R-GemOx-D salvage regimen will be used: Rituximab:
375 mg/m2 on day 1, Gemcitabine: 1000 mg/m2 on day 2 (over 30 minutes) and Oxaliplatin: 100 mg/m2 on day 2 (over 3 hours),
Dexamethasone 20 mg on day 1-3. Cycles should be repeated every 14 days, up to 8 cycles.
Patients who present a complete or partial response, after the salvage therapy, will start the study receiving subcutaneous
Rituximab maintenance at dose of: 1400 mg every 2 months for 2 years; the study treatment will start 6-8 weeks after finishing
the salvage therapy.

End point type	Primary

End point timeframe:

Primary endpoint: Time to relapse/progression (TTP) after achieving a complete or partial response with the (RGemOxD)-induction therapy

End point values	Experimental: subcutaneous rituximab	All		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	19	19		
Units: month				
number (not applicable)	19	19		

Statistical analyses

Statistical analysis title	Complete analisis

Statistical analysis description:

Quantitative variables are described with measures of centralisation and dispersion (Mean, SD, Median, Minimum, Maximum, Q1 and Q3).
Qualitative variables are described by absolute and relative frequencies. In the descriptive analysis of qualitative variables, two columns of percentages are presented, the total percentage (% total) and the valid percentage (% valid).

Comparison groups	Experimental: subcutaneous rituximab v All
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	> 50
Method	Chi-squared
Parameter estimate	PFS
Point estimate	18
Confidence interval	
level	95 %
sides	1-sided
upper limit	19

Notes:

[1] - Non-inferiority of the efficacity of Mainteinment therapy Rituximab intravenous

Secondary: Secondary

End point title	Secondary

End point description:

This is a phase II trial evaluating the role of maintenance with subcutaneous Rituximab in patients with stage II-IV relapsed or
refractory mantle-cell lymphoma with complete or partial response after the administration of a salvage regimen with R-GemOxD.
Before the study start and in order to standardize the results, the same R-GemOx-D salvage regimen will be used: Rituximab:
375 mg/m2 on day 1, Gemcitabine: 1000 mg/m2 on day 2 (over 30 minutes) and Oxaliplatin: 100 mg/m2 on day 2 (over 3 hours),
Dexamethasone 20 mg on day 1-3. Cycles should be repeated every 14 days, up to 8 cycles.
Patients who present a complete or partial response, after the salvage therapy, will start the study receiving subcutaneous
Rituximab maintenance at dose of: 1400 mg every 2 months for 2 years; the study treatment will start 6-8 weeks after finishing
the salvage therapy.

End point type	Secondary

End point timeframe:

Quality of response obtained after subcutaneous Rituximab maintenance.
Progression-Free Survival (PFS)
Overall Survival (OS)
Time to Next Therapy (TTNT)
Value of MRD in the disease outcome
Toxicity

End point values	Experimental: subcutaneous rituximab			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: number				
median (standard deviation)	66 (± 5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: During all the clinic trial	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23
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	2 / 19 (10.53%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences causally related to treatment / all	0 / 2		
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	14 / 19 (73.68%)		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	14 / 19 (73.68%)		
occurrences (all)	14		

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? Yes

Date	Interruption	Restart date
01 June 2017	Missing of efficacity in the treatment	-

Notes:

Limitations and caveats

None reported