Clinical trial results:
GA101-miniCHOP regimen for the treatment of elderly unfit patients with diffuse large B-cell non-Hodgkin's lymphoma.
A phase II study of the Fondazione Italiana Linfomi (FIL).

Summary

EudraCT number	2014-005697-10
Trial protocol	IT
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	22 April 2022
First version publication date	22 April 2022

Trial information

Trial identification

Sponsor protocol code	FIL_GAEL

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fondazione Italiana Linfomi
Sponsor organisation address	Piazza Turati 5, Alessandria , Italy,
Public contact	Segreteria FIL ONLUS, Fondazione Italiana Linfomi ONLUS, 0039 0131206288, segreteria@filinf.it
Scientific contact	Segreteria FIL ONLUS, Fondazione Italiana Linfomi ONLUS, 0039 0131206288, segreteria@filinf.it

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	Interim
Date of interim/final analysis	22 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the activity of GA101-miniCHOP regimen in terms of complete response rate (CRR)

Protection of trial subjects:

Analysis of safety information from clinical studies were crucial for the protection of subjects. The responsible investigator ensured that this study was conducted in agreement with either the Declaration of Helsinki or the laws and regulations of the country, whichever provides the greatest protection of the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
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	Italy: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	0
From 65 to 84 years	26
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

Older adults (≥65 years) with a newly diagnosed DLBCL were considered eligible if they were unfit on the sCGA (comprehensive geriatric assessment).

Pre-assignment

Screening details:

1) Histologically proven CD20 positive Diffuse Large B-cell Lymphoma and Follicular grade IIIB; 2) Age ≥ 65 years; 3) No previous treatment; 4) CGA assessment performed before starting treatment; 5) UNFIT patients; 6) AA Stage I with bulky, II-IV; 7) measurable lesion defined as > 1.5 cm; 8)ECOGPS <3; 9)written informent consent.

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	Single Arm Study

Arm description:

Treatment plan consisted of six cycles of Ga101 (obinutuzumab) -miniCHOP followed by two additional doses of Ga101, every 21 days.

Arm type	Experimental
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:

400 mg/mq, day 1, iv

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

Dosage and administration details:

25 mg/mq, day 1, iv

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:

1 mg, day 1, iv

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

Dosage and administration details: 40 mg/mq, days 1-5, os	
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 1000 mg day 1, iv, every 21 days	

Number of subjects in period 1	Single Arm Study
Started	33
Completed	33

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	33	33	
Age categorical Units: Subjects			
From 65-84 years	26	26	
85 years and over	7	7	
Age continuous Units: years			
median	82		
full range (min-max)	68 to 89	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	18	18	
Stage Units: Subjects			
Stage I-II	6	6	
Stage III-IV	27	27	
Lactate Dehydrogenase Units: Subjects			
LDH <=ULN	10	10	
LDH >ULN	23	23	
ECOG-PS Units: Subjects			
PS 0-1	31	31	
PS 2	1	1	
PS 3	1	1	
International Prognostic Index Units: Subjects			
IPI 1-2	12	12	
IPI 3/5	21	21	
sCGA			
Semplified Comprehensive Geriatric Assessement			
Units: Subjects			
UNFIT	28	28	
FRAIL	5	5	
Hemoglobin Units: g/dL			
median	12.9		
full range (min-max)	8.9 to 15.7	-	
ALC			
Absolute Lymphocyte Count			

Units: 10^9/L			
median	1.2		
full range (min-max)	0.2 to 3.5	-	

Subject analysis sets

Subject analysis set title	Subject analyzed
Subject analysis set type	Full analysis

Subject analysis set description:

From August 2015 to June 2016, 34 patients were enrolled by sixteen Italian centers: one patient was subsequently excluded due to violation of inclusion criteria (Richter syndrome)

Reporting group values	Subject analyzed		
Number of subjects	33		
Age categorical Units: Subjects			
From 65-84 years			
85 years and over			
Age continuous Units: years			
median			
full range (min-max)			
Gender categorical Units: Subjects			
Female	15		
Male	18		
Stage Units: Subjects			
Stage I-II	6		
Stage III-IV	27		
Lactate Dehydrogenase Units: Subjects			
LDH <=ULN	10		
LDH >ULN	23		
ECOG-PS Units: Subjects			
PS 0-1	31		
PS 2	1		
PS 3	1		
International Prognostic Index Units: Subjects			
IPI 1-2	12		
IPI 3/5	21		
sCGA			
Semplified Comprehensive Geriatric Assessement			
Units: Subjects			
UNFIT	28		
FRAIL	5		
Hemoglobin Units: g/dL			
median	12.9		

full range (min-max)	8.9 to 15.7		
ALC			
Absolute Lymphocyte Count			
Units: 10^9/L median full range (min-max)			

End points

End points reporting groups

Reporting group title	Single Arm Study
Reporting group description:	
Treatment plan consisted of six cycles of Ga101 (obinutuzumab) -miniCHOP followed by two additional doses of Ga101, every 21 days.	
Subject analysis set title	Subject analyzed
Subject analysis set type	Full analysis
Subject analysis set description:	
From August 2015 to June 2016, 34 patients were enrolled by sixteen Italian centers: one patient was subsequently excluded due to violation of inclusion criteria (Richter syndrome)	

Primary: Response Rate

End point title	Response Rate
End point description:	
Maximum response attained, according Cheson 1999. Complete remission (CR), partial remission (PR), stable disease (SD), progression disease (PD), not assessed (NA)	
End point type	Primary
End point timeframe:	
8 months from registration	

End point values	Single Arm Study	Subject analyzed		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	33	33		
Units: number of patients				
CR	14	14		
PR	8	8		
SD	2	2		
PD	8	8		
NA	1	1		

Statistical analyses

Statistical analysis title	Rate of complete response
Statistical analysis description:	
Percent frequency	
Comparison groups	Single Arm Study v Subject analyzed
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Frequency percent (%)
Point estimate	42

Confidence interval	
level	95 %
sides	2-sided
lower limit	25
upper limit	61

Secondary: Overall Response (ORR)

End point title	Overall Response (ORR)

End point description:

End point type	Secondary

End point timeframe:

Complete and partial response according to Cheson 1999

End point values	Single Arm Study	Subject analyzed		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	33	33		
Units: number of patients				
ORR	22	22		
Less than ORR	11	11		

Statistical analyses

Statistical analysis title	Overall Response Rate
Comparison groups	Single Arm Study v Subject analyzed
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[1]
Parameter estimate	Frequency percent (%)
Point estimate	67
Confidence interval	
level	95 %
sides	2-sided
lower limit	48
upper limit	82

Notes:

[1] - Frequency of overall response rate (ORR)

Secondary: Overall Survival

End point title	Overall Survival

End point description:

From the date of regsitration in the trial to the date of death for any causes or last clinical contact.

End point type	Secondary
End point timeframe:	
60 months	

End point values	Single Arm Study	Subject analyzed		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	33	33		
Units: Probability of survival at 2-years				
number (confidence interval 68%)	68 (49 to 81)	68 (49 to 81)		

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	Single Arm Study v Subject analyzed
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	2- years OS
Point estimate	68
Confidence interval	
level	95 %
sides	2-sided
lower limit	49
upper limit	81

Secondary: Progression Free Survival

End point title	Progression Free Survival
End point description:	
From the date of registration to the date of prpgression or death for any causes or date of last clinical contact (censored cases).	
End point type	Secondary
End point timeframe:	
60 months	

End point values	Single Arm Study	Subject analyzed		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	33	33		
Units: Probability at 2-years				
number (confidence interval 49%)	49 (28 to 67)	49 (28 to 67)		

Statistical analyses

Statistical analysis title	Progression Free Survival
Comparison groups	Single Arm Study v Subject analyzed
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	2-year probability
Point estimate	49
Confidence interval	
level	95 %
sides	2-sided
lower limit	28
upper limit	67

Adverse events

Adverse events information

Timeframe for reporting adverse events:

60 months

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Single arm study

Reporting group description: -

Serious adverse events	Single arm study		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 33 (18.18%)		
number of deaths (all causes)	10		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Congestive heart failure			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 1		
Respiratory, thoracic and mediastinal disorders			
Obstructive chronic bronchopneumopathy			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Lumbar pain, vertbral collapse			

subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
fever, sepsis			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Single arm study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 33 (84.85%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	2 / 33 (6.06%)		
occurrences (all)	2		
Vascular disorders			
Vascular disorder			
subjects affected / exposed	1 / 33 (3.03%)		
occurrences (all)	1		
General disorders and administration site conditions			
General disorder			
subjects affected / exposed	9 / 33 (27.27%)		
occurrences (all)	9		
Investigations			
Investigations			
subjects affected / exposed	3 / 33 (9.09%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			

Procedural complication subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3		
Cardiac disorders Cardiac disorder subjects affected / exposed occurrences (all)	5 / 33 (15.15%) 5		
Nervous system disorders Nervous system disorder subjects affected / exposed occurrences (all)	7 / 33 (21.21%) 7		
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 6 / 33 (18.18%) 6 4 / 33 (12.12%) 4 15 / 33 (45.45%) 15 11 / 33 (33.33%) 11		
Gastrointestinal disorders Gastrointestinal disorder subjects affected / exposed occurrences (all)	13 / 33 (39.39%) 13		
Hepatobiliary disorders Hepatobiliary disorder subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Renal and urinary disorders Renal disorder subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2		
Musculoskeletal and connective tissue disorders			

Musculoskeletal disorder subjects affected / exposed occurrences (all)	8 / 33 (24.24%) 8		
Infections and infestations Infections subjects affected / exposed occurrences (all)	10 / 33 (30.30%) 10		
Metabolism and nutrition disorders Metabolism disorder subjects affected / exposed occurrences (all)	8 / 33 (24.24%) 8		

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
28 February 2017	The study was early interrupted at the interim analysis becouse the complete remission rate less than expected. Enrolled 33 patients in place of 78 planned patients.	-

Notes:

Limitations and caveats

None reported