Clinical trial results:
Multicenter phase II single arm open-label study on the feasibility, safety and efficacy of combination of CHOP-21 supplemented with Obinutuzumab and Ibrutinib in untreated young high risk Diffuse Large B-cell Lymphoma (DLBCL) patients.

Summary

EudraCT number	2015-005273-20
Trial protocol	IT
Global end of trial date	17 February 2017

Results information

Result version number	v1 (current)
This version publication date	11 October 2022
First version publication date	11 October 2022

Trial information

Trial identification

Sponsor protocol code	FIL-GALILEO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02670317
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fondazione Italiana Linfomi (FIL) ONLUS
Sponsor organisation address	Piazza Turati 5, Alessandria, Italy,
Public contact	Segreteria, Fondazione Italiana Linfomi Onlus, +39 0131/033151, segreteriadirezione@filinf.it
Scientific contact	Segreteria, Fondazione Italiana Linfomi Onlus, +39 0131/033151, segreteriadirezione@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	Final
Date of interim/final analysis	03 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of G-CHOP-21 in combination with Ibrutinib in terms of 2-yrs PFS; To evaluate the safety of G-CHOP-21 in combination with Ibrutinib (extra-hematologic toxicity = grade 3 or treatment interruption for safety reasons or any toxic death during the 6 cycles of treatment).

Protection of trial subjects:

A subject must be discontinued from study treatment in case of:
- completed treatment as per protocol
- Patient withdraw consent to participate
- the investigator believes that for safety reasons it is in the best interest of the subject to discontinue the treatment
- disease progression at any time
- occurrence of an unacceptable adverse event (> grade 3 toxicity for > 2 weeks)
If the treatment is discontinued for more than 3 weeks patient is withdrawn from study protocol treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 September 2016
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: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

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)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One patient recruited in Italy from September 2, 2016, with date of last completed February 17, 2017 (date of early closure of study).

Pre-assignment

Screening details:

Patients (18-60 years) with poor-prognosis (age-adjusted International Prognostic Index, aaIPI, 2 or 3) newly diagnosed DLBCL.
All patients must satisfy all the inclusion criteria and none of exclusion criteria.

Period 1

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

Arms

Arm title	Single arm

Arm description:

One single arm.
Patients will receive a maximum of 6 courses of G-CHOP-21 followed by 2 doses of Obinutuzumab in combination with Ibrutinib.

Arm type	Single arm study
Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

560 mg (4 x 140mg capsules) per os (PO) QD, day 1-126 once daily

Investigational medicinal product name	Obinutuzumab (G)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg, intra venous (IV) days 1, 8, 15, 21, 42, 63, 84, 105, 126,147.
It is allowed to split the first Obinutuzumab infusion over 2 days (day 1 and 2) if the patient is at increased risk for infusion related reaction (IRR) (high tumor burden, high peripheral lymphocyte count or other medical conditions).

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cyclophosphamide: 750 mg/m2, IV on day 1

CHOP (Cyclophosphamide, Adriamycin, Vincristine, Prednisone) will be administered according to the standard preparation and infusion procedures at each investigational site and at least 30 minutes after the Obinutuzumab infusion. CHOP-21: days 1, 21, 42, 63, 84, 105

Investigational medicinal product name	Adriamycin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Adriamycin: 50 mg/m2, IV on day 1

CHOP (Cyclophosphamide, Adriamycin, Vincristine, Prednisone) will be administered according to the standard preparation and infusion procedures at each investigational site and at least 30 minutes after the Obinutuzumab infusion. CHOP-21: days 1, 21, 42, 63, 84, 105

Investigational medicinal product name	Vincristine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Vincristine: 1.4 mg/m2, IV on day 1, (max 2 mg)

CHOP (Cyclophosphamide, Adriamycin, Vincristine, Prednisone) will be administered according to the standard preparation and infusion procedures at each investigational site and at least 30 minutes after the Obinutuzumab infusion. CHOP-21: days 1, 21, 42, 63, 84, 105

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

Dosage and administration details:

Prednisone: 100 mg/day, PO on day 1-5

CHOP (Cyclophosphamide, Adriamycin, Vincristine, Prednisone) will be administered according to the standard preparation and infusion procedures at each investigational site and at least 30 minutes after the Obinutuzumab infusion. CHOP-21: days 1, 21, 42, 63, 84, 105

Number of subjects in period 1	Single arm
Started	1
Completed	1

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	1	1	
Age categorical Units: Subjects			
Adults (18-64 years)	1	1	
Gender categorical Units: Subjects			
Female	1	1	

End points

End points reporting groups

Reporting group title	Single arm

Reporting group description:

One single arm.
Patients will receive a maximum of 6 courses of G-CHOP-21 followed by 2 doses of Obinutuzumab in combination with Ibrutinib.

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)[1]

End point description:

PFS will be defined as the time between the date of enrolment and the date of disease progression, relapse or death from any cause.

End point type	Primary

End point timeframe:

2 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only one patient was enrolled, the study is officially closed by 17/2/2017. Analyzes not carried out.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Probability				
number (confidence interval 95%)	(to)			

Notes:

[2] - Only one patient was enrolled,the study is officially closed by 17/2/2017. Analyzes not carried out

Statistical analyses

No statistical analyses for this end point

Primary: Clinical relevant toxicity

End point title	Clinical relevant toxicity[3]

End point description:

To evaluate the safety of G-CHOP-21 in combination with Ibrutinib in terms of proportion of patients experiencing grade 3 or greater extrahematologic toxicity or treatment interruption for safety reasons or any toxic death during the 6 cycles of treatment.
Clinical relevant toxicity will be defined as the proportion of patients experiencing a grade 3 or greater extra-hematologic toxicity or treatment interruption for safety reasons due to patient or clinical decisions or any toxic death during the 6 cycles of treatment.

End point type	Primary

End point timeframe:

5 months of treatment

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only one patient was enrolled, the study is officially closed by 17/2/2017. Analyzes not

carried out.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Subject				

Notes:

[4] - Only one patient was enrolled,the study is officially closed by 17/2/2017. Analyzes not carried out.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 2 years	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0
Reporting groups	
Reporting group title	Single arm

Reporting group description: -

Serious adverse events	Single arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Single arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fever			
subjects affected / exposed	1 / 1 (100.00%)		
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? Yes

Date	Interruption	Restart date
17 February 2017	The reasons for the early closure are as follows. The association Obinutuzamab - CHOP, investigated by the study, cannot have clinical development in large B lymphomas cells in the forefront. The results of the study were reported at the ASH 2016 meeting Randomized Goya (Rituximab -CHOP versus Obinutuzumab-CHOP), conducted on 1418 patients. The study results showed no significant survival advantage disease-free (PFS) and overall survival (OS) by the replacement of Rituximab with Obinutuzumab (Vitolo et al. - "Obinutuzumab or Rituximab plus CHOP in patients with previously untreated diffuse large B-cell lymhoma: final results from an open-label, randomized phase 3 study (GOYA) "- 58th ASH Meeting San Diego 2016 - Abstract 470). Therefore, there not will be expected neither experimental developments nor further approvals by the competent authorities for the use of the association Obinutuzumab-CHOP in large-cell B lymphomas. For this reason, the addition of the drug Ibrutinib to the Obinutuzumab-CHOP association no longer has any logic and interest in the future clinical practice. The study is officially closed starting from 17/2/2017. Only 1 patient was enrolled in the study (coordinating center), and the data collection and follow-up analysis will be guaranteed.	-

Notes:

Limitations and caveats

None reported