Clinical trial results:
A phase II study of SGN-35 (brentuximab vedotin) of patients with relapsed or refractory Primary mediastinal large B-cell lymphoma (PMLBCL).

Summary

EudraCT number	2012-000735-27
Trial protocol	IT
Global end of trial date	14 July 2016

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_SGN01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02423291
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	Secretary, FONDAZIONE ITALIANA LINFOMI ONLUS, 0039 0131/033151, segreteriadirezione@filinf.it
Scientific contact	Secretary, FONDAZIONE ITALIANA LINFOMI ONLUS, 0039 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	17 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 July 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine the antitumor efficacy of single-agent Brentuximab vedotin (1.8 mg/kg administered intravenously every 3 weeks) as measured by the overall objective response rate in patients with relapsed or refractory primary mediastinal large B-cell lymphoma.

Protection of trial subjects:

A patient’s treatment with Brentuximab vedotin may be discontinued for any of the following reasons:
• Disease progression.
• Stable disease or better and completed 16 treatment cycles.
• The Investigator or patient deems it in the patient’s best interest to discontinue. The reason justifying study treatment withdrawal must be documented in the CRF.
Patients who discontinue from study treatment will remain on study for follow-up unless they withdraw consent. All patients who receive at least 1 dose of study drug will be followed every 12 weeks until death or study closure, whichever comes first.

Intrapatient dose reduction to 1.2 mg/kg will be allowed depending on the type and severity of toxicity. The start of the next cycle may be delayed for up to 3 weeks if additional time is required for the patient to recover from study treatment-associated toxicity experienced during the current cycle. Delays of greater than 3 weeks are prohibited without approval of the Sponsor.
Doses reduced for drug-related toxicity should generally not be re-escalated. However, intrapatient re-escalation to the previous dose level may be permitted at the discretion of the Investigator.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 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	Italy: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	13
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Fifteen patients recruited in Italy from 2 October 2013 , with date of last completed at 8 October 2015. No screening failure, no waivers. The Sponsor and the Study Coordinator decided to stop the trial due to drug inefficacy on 14/Jul/2016 (last enrollment on 30/Jun/2015).

Pre-assignment

Screening details:

Study Population Eligible patients are those with relapsed or refractory primary mediastinal large B-cell lymphoma.
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:

This is a single-arm, open-label, multicenter, Phase 2 clinical trial to evaluate the efficacy and safety of Brentuximab vedotin as a single agent in patients with relapsed or refractory PMLBCL who have previously received a first line of treatment with chemotherapy or immunotherapy. All treated patients will receive 1.8 mg/kg Brentuximab vedotin administered as a single outpatient IV infusion on Day 1 of each 21-day treatment cycle. Patients may continue on study treatment until disease progression or unacceptable toxicity. Patients who achieve stable disease or better as assessed by investigator should receive a minimum of 8, but no more than 16 cycles of study treatment.

Arm type	Single arm study
Investigational medicinal product name	Brentuximab Vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Brentuximab vedotin, 1.8 mg/kg, administered via outpatient IV infusion on Day 1 of each 21-day cycle.

Number of subjects in period 1	Single arm
Started	15
Completed	0
Not completed	15
Adverse Event	1
Lack of efficacy	14

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adults (18-64 years)	13	13	
From 65-84 years	2	2	
Age continuous Units: years			
arithmetic mean	37		
standard deviation	± 18.63	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	5	5	

End points

End points reporting groups

Reporting group title	Single arm

Reporting group description:

This is a single-arm, open-label, multicenter, Phase 2 clinical trial to evaluate the efficacy and safety of Brentuximab vedotin as a single agent in patients with relapsed or refractory PMLBCL who have previously received a first line of treatment with chemotherapy or immunotherapy. All treated patients will receive 1.8 mg/kg Brentuximab vedotin administered as a single outpatient IV infusion on Day 1 of each 21-day treatment cycle. Patients may continue on study treatment until disease progression or unacceptable toxicity. Patients who achieve stable disease or better as assessed by investigator should receive a minimum of 8, but no more than 16 cycles of study treatment.

Primary: Overall Objective Response Rate in Patients With Relapsed or Refractory PMLBCL

End point title	Overall Objective Response Rate in Patients With Relapsed or Refractory PMLBCL[1]

End point description:

The antitumor efficacy of single-agent Brentuximab vedotin (1.8 mg/kg administered intravenously every 3 weeks) as measured by the overall objective response rate in patients with relapsed or refractory primary mediastinal large B-cell lymphoma was determined using Cheson BD, Pfistner B, Juweid ME, et al. "Revised response criteria for malignant lymphoma". J Clin Oncol. 2007 Feb 10;25(5):579-586.Treatment response was assessed by dedicated spiral CT scan of neck, chest, neck, abdomen, and pelvis and PET scans performed at protocol-specified time points. Clinical response of progressive disease (PD), stable disease (SD), partial remission (PR), or complete remission (CR) will be determined at each assessment.

End point type	Primary

End point timeframe:

42 months

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: Trial was closed due to drug inefficacy on 14/Jul/2016 (last enrollment on 30/Jun/2015).

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	15[2]			
Units: Subject				
Quick PD	11			
PD after 1 cycle	1			
PD after 2 cycle	1			
PR	1			
SAE not related to drug	1			

Notes:

[2] - Trial was closed due to drug inefficacy on 14/Jul/2016 (last enrollment on 30/Jun/2015).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
All Study Duration (3 years, 10 months)	
Adverse event reporting additional description:	
We used the Common Terminology Criteria for Adverse Events v. 4.0 (CTCAE) for the coding of adverse events.	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups	
Reporting group title	Single arm
Reporting group description:	
This is a single-arm, open-label, multicenter, Phase 2 clinical trial to evaluate the efficacy and safety of Brentuximab vedotin as a single agent in patients with relapsed or refractory PMLBCL who have previously received a first line of treatment with chemotherapy or immunotherapy. All treated patients will receive 1.8 mg/kg Brentuximab vedotin administered as a single outpatient IV infusion on Day 1 of each 21-day treatment cycle. Patients may continue on study treatment until disease progression or unacceptable toxicity. Patients who achieve stable disease or better as assessed by investigator should receive a minimum of 8, but no more than 16 cycles of study treatment.	

Serious adverse events	Single arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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	15 / 15 (100.00%)		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nervous system disorders			
Peripheral neuropathy (NEC)			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Leukopenia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Granulocytopenia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Thrombocytopenia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Intestinal perforation			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Erythema subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 September 2013	Seattle Genetics communication for the inclusion of a new side effect in the Information for patients enrolled in protocols with Brentuximab Vedotin (SGN-35)
22 June 2014	Variation of the Coordinator Investigator Dr. Vittorio Stefoni instead of Prof. Pier Luigi Zinzani; updating of parts relating to toxicity and relative modification of drug doses, new pharmaceutical company pharmacovigilance contacts, correction of marginal typos to the protocol, updating of the list of centers, changes to the contract based on requests from the CE of Reggio Emilia and Bologna.
30 October 2014	Notice from Millennium Takeda regarding the transition of the drug Adcetris® Brentuximab Vedotin (SGN-35) from experimental to commercial for experimental use. ONLY FOR AIFA AND COORDINATOR
03 September 2015	New IB, new FIL / Millennium contract, new consents.
19 February 2016	New IB and related changes to consents.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 July 2016	Fifteen of the 20 expected patients were enrolled; in particular, no patients have been enrolled in the past 12 months. This finding is likely related to the preliminary clinical findings. Based on these data, the study is closed early due to the ineffectiveness of the drug in this pathology.	-

Notes:

Limitations and caveats

None reported