Clinical trial results:
Phase II clinical trial of immunotherapy with Rituximab and autologous effector lymphocytes in patients with non-Hodgkin follicular lymphoma in response to first line chemotherapy

Summary

EudraCT number	2009-017829-19
Trial protocol	ES
Global end of trial date	30 November 2020

Results information

Result version number	v1 (current)
This version publication date	27 November 2021
First version publication date	27 November 2021

Trial information

Trial identification

Sponsor protocol code	LFNK

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01329354
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clínica Universidad de Navarra/Universidad de Navarra
Sponsor organisation address	Avenida Pío XII, 36, Pamplona, Spain, 31008
Public contact	UCICEC, Clínica Universidad de Navarra, +34 948255400, ucicec@unav.es
Scientific contact	UCICEC, Clínica Universidad de Navarra, +34 948255400, ucicec@unav.es

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	22 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 November 2020
Global end of trial reached?	Yes
Global end of trial date	30 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the impact of treatment on progression-free survival

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 March 2011
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: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

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)	23
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with follicular lymphoma with criteria to start maintenance treatment, who have received induction treatment according to the standard R-CHOP chemotherapy regimen, were recruited.

Pre-assignment

Screening details:

Patients aged 18-75 years with histologically confirmed Grade I, II or IIIa CD20+ FL, ready to start maintenance therapy with rituximab after achieving a partial response (PR) or complete response (CR) subsequent to R-CHOP.

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Experimental group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	LAK cells
Investigational medicinal product code	
Other name	Ex vivo expanded lymphokine-activated killer (LAK) cells
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

500 millions

Number of subjects in period 1	Experimental group
Started	26
Completed	20
Not completed	6
Consent withdrawn by subject	1
Screening failure	2
Protocol deviation	3

Baseline characteristics

Reporting groups

Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	26	26	
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)	23	23	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	10	10	
Male	16	16	

End points

End points reporting groups

Reporting group title	Experimental group

Reporting group description: -

Primary: Progression free survival rate

End point title	Progression free survival rate[1]

End point description:

Percentage of patients without progression observed during the 5 years of follow-up period

End point type	Primary

End point timeframe:

Five years after the end of treatment

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: A Kaplan-Meier curve was generated.

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percent of patients without progression				
number (not applicable)	80			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious AEs and SAEs were collected during the treatment period and for a minimun of 30 days following the last dose of study treatment. Treatment-related SAEs were collected and evaluated from study start until 60 month after last dose of treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18-1

Reporting groups

Reporting group title	Experimental group

Reporting group description: -

Serious adverse events	Experimental group		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 20 (15.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Female sterilisation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatic surgery			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urosepsis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostatitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Experimental group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vascular disorders			
Lymphoedema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Deep vein thrombosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Surgical and medical procedures			
Prostate surgery			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hysterectomy			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	12		
Heat in the join of the administration area			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Peripheral edema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General discomfort			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Erectile dysfunction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Prostatitis			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Cold			
subjects affected / exposed	10 / 20 (50.00%)		
occurrences (all)	15		
Nasal congestion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dysphonia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dyspnea exertional			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
COPD			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Productive cough			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Roncus			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	6		
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Depression subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Insomnia subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 3		
Cardiac disorders Ventricular extrasystoles subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Dizziness subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Dizziness exertional subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Neuropathy peripheral subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Paraesthesia subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 5		
Polyneuropathy subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	5		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Keratitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Exfoliation syndrome			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	7		
Diverticulitis/Colitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Dental pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain lower			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Constipation			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Inguinal hernia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Aphthous ulcer			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Mouth ulceration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Seborrheic dermatitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
Erythema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eruption			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Pruritus anal			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	4		
Bleeding from the bladder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 20 (45.00%)		
occurrences (all)	12		
Arthritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Bursitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Neck pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	4		
Jaw pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pain in a limb			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Limb discomfort			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Rotator cuff syndrome			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Infections and infestations			
Dental abscess			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Cystitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Conjunctivitis bacterial			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Furuncle			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		

Ophthalmic herpes				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Oral herpes				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Herpes zoster				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	11 / 20 (55.00%)			
occurrences (all)	15			
Urinary tract infection				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Dental infection				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Fungal infection				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	2			
Pneumonia				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Pyelonephritis chronic				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			

Tonsillitis subjects affected / exposed occurrences (all) Urosepsis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Dyslipidaemia subjects affected / exposed occurrences (all) Hypercholesterolaemia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 2 / 20 (10.00%) 2 1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 July 2010	Add thyroid function and autoimmunity tests at certain visits (Protocol v2)
04 February 2011	Adapt protocol to new standard treatment (Protocol v3) Modify ICF to clarify financial compensation (ICF v3)
04 March 2011	Add sites. Remove references to CRO (Protocol v4)
02 November 2011	Restructuring objectives. Sample size decrease. Errata correction (Protocol v5)
25 June 2012	Change of sponsor. Add the ability to draw blood and LAK infusion is done in referral centers (Protocol v7, ICF v4)
21 June 2013	Changes in the IMPD (IMPD v3)
29 October 2013	Change of PI in one of the sites
02 June 2014	Change in IB (IB v2) Eliminate the need to collect AEs and concomitant medications in follow-up and to report SAEs not related to the investigational product. Add intermediate analysis after completion of treatment of all patients (Protocol v8)
04 January 2016	Change of PI in one of the sites
10 November 2016	Change of PI in one of the sites

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32130737