



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 minimum of 30 days following the last dose of study treatment. Treatment-related SAEs were collected and evaluated from study start until 60 months 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 occurrences (all) | 1 / 20 (5.00%) 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 occurrences (all) | 3 / 20 (15.00%) 5 | | |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 3 / 20 (15.00%) 3 | | |
| Eye disorders Blepharitis subjects affected / exposed occurrences (all) Keratitis subjects affected / exposed occurrences (all) Exfoliation syndrome subjects affected / exposed occurrences (all) | 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Diverticulitis/Colitis subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Dental pain subjects affected / exposed occurrences (all) Abdominal pain lower subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation | 5 / 20 (25.00%) 7 1 / 20 (5.00%) 1 3 / 20 (15.00%) 4 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 | | |

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

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