

Purine-Alkylator Combination In Follicular lymphoma Immuno-Chemotherapy for Older patients

Submission date 22/01/2009	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 03/03/2009	Overall study status Completed	☐ Statistical analysis plan ☐ Results
Last Edited 20/03/2020	Condition category Cancer	☐ Individual participant data ☐ Record updated in last year

Plain English summary of protocol

<http://www.cancerhelp.org.uk/trials/trials-search/trial-looking-rituximab-chemotherapy-treatment-follicular-lymphoma-elderly-patients-pacifico>

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

ClinicalTrials.gov (NCT)

NCT01303887

Clinical Trials Information System (CTIS)

Study information

Scientific Title

Purine-alkylator combination in follicular lymphoma immuno-chemotherapy for older patients: a phase III randomised controlled trial

Acronym

PACIFICO

Study objectives

To investigate if the new immuno-chemotherapy combination regimen rituximab, fludarabine and cyclophosphamide (R-FC) improves rate of progression-free survival in older patients (aged 60+ years) when compared to the current gold standard treatment of rituximab, cyclophosphamide, vincristine and prednisone (R-CVP), without being significantly more toxic.

Patients aged less than 60 years will be considered for the trial if more intensive chemotherapy is considered inappropriate due to co-morbidity.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Added 09/03/2010:

1. Liverpool Adult Research Ethics Committee (MREC), 19/06/2009, ref: 09/H1005/29
2. Medicines and Healthcare products Regulatory Agency (MHRA), 03/07/2009, ref: 04196/0014/001-0001

Primary study design

Interventional

Study design

Phase III randomised controlled trial

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Follicular lymphoma

Interventions

Control arm (R-CVP):

Rituximab 375 mg/m² intravenous (IV) day 1, cyclophosphamide 750 mg/m² IV day 1, vincristine 1.4 mg/m² IV day 1, prednisolone 40 mg/m² orally (PO) day 1 - 5, repeated every 21 days for 8 cycles.

Experimental arm (R-FC):

Rituximab 375 mg/m² IV day 1, fludarabine 40 mg/m² PO day 1 - 3, cyclophosphamide 250 mg/m² PO day 1 - 3, repeated every 21 days for 4 cycles followed by rituximab 375 mg/m² alone for 4 further cycles.

Rituximab maintenance:

All patients who have achieved a complete response (CR) or partial response (PR) to induction therapy will receive rituximab maintenance (375 mg/m² every 2 months for 2 years).

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Rituximab, fludarabine, cyclophosphamide, vincristine, prednisone

Primary outcome(s)

1. Progression free survival (PFS): length of PFS defined as number of days between date of randomisation and the date of progression, date of death from any cause or the date last seen progression free (censor date)
2. Toxicity: grade 3 - 4 infection will be used as the toxicity end-point. Toxicity will be measured according to standard National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0 following each cycle of treatment and at each subsequent follow-up visit.

Key secondary outcome(s)

1. Response rates (overall, complete and partial) following initial therapy - assessment made following initial therapy
2. Response rates following maintenance therapy - assessment made following maintenance therapy
3. Response duration - time to event outcome
4. Overall survival - time to event outcome
5. Time to treatment failure - time to event outcome
6. Time-to-next treatment - time to event outcome
7. Number of treatment cycles delivered - assessment made following second-line therapy
8. Cumulative dose of individual drugs administered - assessment made following initial therapy
9. Quality of life - EORTC QLQ C-30, EQ-5D and EQ-VAS questionnaires will be completed at various time points during the course of treatment and follow up
10. Cost effectiveness - will be assessed at various time points during the course of treatment and follow up
11. Response to second-line therapy - assessment made following second-line therapy

Completion date

01/07/2019

Eligibility

Key inclusion criteria

1. Histologically confirmed follicular lymphoma, grade 1, 2, and 3a with material available for central review
2. Ann Arbor stage II - IV, i.e. all patients except those with strictly localised disease for whom local radiotherapy would be appropriate. Lymph nodes should be considered pathologically enlarged if the long axis is more than 1.5 cm regardless of the short axis. If a lymph node has a long axis of 1.1 to 1.5 cm, it should only be considered abnormal if its short axis is more than 1.0 cm.
3. Aged 60 years or over (or less than 60 but more intensive chemotherapy considered inappropriate due to co-morbidity), either sex
4. At least one of the following British National Lymphoma Investigation (BNLI) criteria for initiation of treatment:
 - 4.1. Rapid generalised disease progression in the preceding 3 months
 - 4.2. Life threatening organ involvement
 - 4.3. Renal or macroscopic liver infiltration
 - 4.4. Bone lesions
 - 4.5. Presence of systemic symptoms or pruritus
 - 4.6. Haemoglobin less than 10 g/dL or whole blood cell count (WBC) less than $3.0 \times 10^9/L$ or platelet count less than $100 \times 10^9/L$ due to marrow involvement
5. Adequate haematological function (unless abnormalities are related to lymphoma infiltration of the bone marrow) within 28 days prior to registration:
 - 5.1. Haemoglobin greater than or equal to 8.0 g/dL
 - 5.2. Absolute neutrophil count (ANC) greater than or equal to $1.5 \times 10^9/L$
 - 5.3. Platelet count greater than or equal to $100 \times 10^9/L$
6. Written informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Senior

Sex

All

Key exclusion criteria

1. Prior anti-lymphoma treatment
2. Overt transformation to diffuse large B-cell lymphoma
3. World Health Organization (WHO) performance status 3 or 4
4. Creatinine clearance less than 30 ml/min
5. Serum bilirubin more than twice upper limit of normal (unless due to lymphoma)
6. Life expectancy less than 12 months
7. Infection with human immunodeficiency virus (HIV), hepatitis B or hepatitis C. Patients with any serological evidence of current or past exposure to HIV, hepatitis B or hepatitis C are excluded unless the serological findings are clearly due to vaccination.
8. Allergy to murine proteins
9. Grade 3b follicular lymphoma
10. Presence or history of CNS disease (either CNS lymphoma or lymphomatous meningitis)

11. Patients regularly taking corticosteroids during the last 4 weeks, unless administered at a dose equivalent to less than 20 mg/day prednisolone
12. Patients with prior or concomitant malignancies except non-melanoma skin cancer or adequately treated in situ cervical cancer
13. Major surgery (excluding lymph node biopsy) within 28 days prior to registration
14. Serious underlying medical conditions, which could impair the ability of the patient to participate in the trial (e.g. ongoing infection, uncontrolled diabetes mellitus, gastric ulcers, active autoimmune disease)
15. Treatment within a clinical trial within 30 days prior to trial entry
16. Any other co-existing medical or psychological condition that will preclude participation in the study or compromise ability to give informed consent
17. Adult patient under tutelage (not competent to sign informed consent)

Date of first enrolment

01/05/2009

Date of final enrolment

01/05/2017

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

University of Liverpool School of Cancer Studies

Liverpool

United Kingdom

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Sponsor information

Organisation

University of Liverpool (UK)

ROR

<https://ror.org/04xs57h96>

Funder(s)

Funder type

Charity

Funder Name

Cancer Research UK (CRUK) (UK) (ref: C18029/A10015)

Alternative Name(s)

CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type

Private sector organisation

Funding Body Subtype

Other non-profit organizations

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary****Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes