ISRCTN99217456 https://doi.org/10.1186/ISRCTN99217456

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

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

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/trials-search/trial-looking-rituximab-chemotherapy-treatment-follicular-lymphoma-elderly-patients-pacifico

Study website
http://www.lctu.org.uk/

Contact information

Type(s)
Scientific

Contact name
Prof Andrew Pettitt

Contact details
University of Liverpool School of Cancer Studies
Division of Haematology
Level 2 Duncan Building
Royal Liverpool University Hospital
Daulby Street
Liverpool
United Kingdom
L69 3GA
+44 (0)151 706 4363
arp@liv.ac.uk

Additional identifiers

EudraCT/CTIS number

2008-004759-31

IRAS number

ClinicalTrials.gov number
NCT01303887

Secondary identifying numbers
N/A

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

Study design
Phase III randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Follicular lymphoma

Interventions
Control arm (R-CVP):
Rituximab 375 mg/m^2 intravenous (IV) day 1, cyclophosphamide 750 mg/m^2 IV day 1, vincristine 1.4 mg/m^2 IV day 1, prednisolone 40 mg/m^2 orally (PO) day 1 - 5, repeated every 21 days for 8 cycles.

Experimental arm (R-FC):
Rituximab 375 mg/m^2 IV day 1, fludarabine 40 mg/m^2 PO day 1 - 3, cyclophosphamide 250 mg /m^2 PO day 1 - 3, repeated every 21 days for 4 cycles followed by rituximab 375 mg/m^2 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/m^2 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 measure
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.

Secondary outcome measures
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

Overall study start date
01/05/2009

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 of 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 × 10^9/L or platelet count less than 100 × 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 x 10^9/L
5.3. Platelet count greater than or equal to 100 x 10^9/L
6. Written informed consent

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
680

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
England

United Kingdom

Study participating centre
University of Liverpool School of Cancer Studies
Liverpool
United Kingdom
L69 3GA

Sponsor information

Organisation
University of Liverpool (UK)

Sponsor details
Research and Business Services
The Foresight Centre
3 Brownlow Street
Liverpool
England
United Kingdom
L69 3GL

Sponsor type
University/education

Website
http://www.liv.ac.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, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

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