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CLL6 (Roche): a randomised, phase II trial of fludarabine, cyclophosphamide and rituximab (FCR) with or without mitoxantrone in previously untreated chronic lymphocytic leukaemia

Submission date 17/06/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 02/10/2008	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 27/07/2022	**Condition category** Cancer	[_] Individual participant data

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/trials-search/a-trial-looking-at-treatment-for-people-with-newly-diagnosed-chronic-lymphocytic-leukaemia

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HM08/8625

Study information

Scientific Title
CLL6 (Roche): a randomised, phase II trial of fludarabine, cyclophosphamide and rituximab (FCR) with or without mitoxantrone in previously untreated chronic lymphocytic leukaemia

Acronym
CLL6 (Roche)

Study objectives
The trial is intended to compare the complete remission rates of fludarabine, cyclophosphamide and rituximab (FCR) with or without mitoxantrone (M) in patients with previously untreated chronic lymphocytic leukaemia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leeds (West) Research Ethics Committee, 09/02/2009, ref: 08/H1307/135

Study design
Phase II multi-centre randomised controlled open parallel-group trial

Primary study design
Interventional

Secondary study design
Randomised parallel 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
Chronic lymphocytic leukaemia (CLL)

Interventions

This trial aims to recruit 218 patients over 18 months. Patients will be randomised to receive six cycles of either FCR or FCM-R. Cycles of FCR and FCM-R are reported every 28 days for a total of six courses. Each cycle is repeated every 28 days. However treatment is administered during each cycle as per the following schedule:

Patients randomised to receive fludarabine, cyclophosphamide and rituximab (FCR) will receive:
Fludarabine (oral): 24 mg/m^2/day on days 1 to 5
Cyclophosphamide (oral): 150 mg/m^2/day on days 1 to 5
Rituximab (IV): 375 mg/m^2 on day 1 (cycle 1)
Rituximab (IV): 500 mg/m^2 on day 1 (cycle 2 to 6)

Patients randomised to receive fludarabine, cyclophosphamide, rituximab and mitoxantrone (FCM-R) will receive:
Fludarabine (oral): 24 mg/m^2/day on days 1 to 5
Cyclophosphamide (oral): 150 mg/m^2/day on days 1 to 5
Rituximab (IV): 375 mg/m^2 on day 1 (cycle 1)
Rituximab (IV): 500 mg/m^2 on day 1 (cycle 2 to 6)
Mitoxantrone (IV): 6 mg/m^2/day on day 1

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Fludarabine, cyclophosphamide, rituximab, mitoxantrone

Primary outcome measure
Proportion of patients achieving a complete response (CR) at three months post end-of-treatment as specified by the IWCLL criteria

Secondary outcome measures
1. Proportion of patients with undetectable minimal residual disease, measured at three months post-end-of-treatment
2. Overall response rate defined as complete or partial remission by the IWCLL criteria, measured at three months post-end-of-treatment
3. Progression free survival at two years
4. Overall survival at two years
5. Safety and toxicity, measured at two years after randomisation

Overall study start date
01/01/2009

Completion date
01/07/2012

Eligibility

Key inclusion criteria

1. Both males and females, at least 18 years old
2. B-cell chronic lymphocytic leukaemia (B-CLL) with a characteristic immunophenotype
3. Binet's Stages B, C or Progressive A
4. Requirement for therapy as defined by the International Workshop on Chronic Lymphocytic Leukemia (IWCLL) criteria (must meet one of the following criteria: evidence of progressive marrow failure as manifested by the development of, or worsening of, anaemia and/or thrombocytopenia)
5. Massive (i.e. 6 cm below the left costal margin) or progressive or symptomatic splenomegaly
6. Massive nodes (i.e. 10 cm in longest diameter) or progressive or sypmtomatic lymphodenopathy
7. Progressive lymphocytosis with an increase of more than 50% over a 2-month period or lymphocyte doubling time (LDT) of less than 6 months as long as the lymphocyte count is over 30 x 10^9/L
8. A minimum of any one of the following disease-related symptoms must be present:
8.1. Unitentional weight loss more than or equal to 10% within the previous 6 months
8.2. Significant fatigue (i.e. Eastern Cooperative Oncology Group performance status 2 or worse; cannot work or unable to perform usual activities)
8.4. Fevers of greater than 38°C for two or more weeks without other evidence of infection
8.5. Night sweats for more than one month without evidence of infection
9. No prior therapy for CLL
10. Able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
218

Total final enrolment
215

Key exclusion criteria
1. Prior therapy for CLL
2. Active infection
3. Past history of anaphylaxis following exposure to rat or mouse derived complementarity-determining regions (CDR)-grafted humanised monoclonal antibodies
4. Pregnancy, lactation or women of child bearing potential unwilling to use medically approved contraception whilst receiving treatment
5. Men whose partners are capable of having children but who are not willing to use appropriate medically approved contraception during the study, unless they are surgically sterile
6. Central nervous system (CNS) involvement with CLL
7. Mantle cell lymphoma

8. Other severe, concurrent disease or mental disorders
9. Known human immunodeficiency virus (HIV) positive
10. Patient has active or prior hepatitis B or C
11. Active secondary malignancy excluding basal cell lymphoma
12. Persisting severe pancytopenia (neutrophils less than 0.5 x 10^9/L or platelets less than 50 x 10^9/L), trasfusion dependent anaemia and active haemolysis
13. Patients with a creatinine clearance of less than 30 ml/min (either measured or derived by the Cockroft formula)

Date of first enrolment
01/06/2009

Date of final enrolment
30/03/2012

Locations

Countries of recruitment
England

Ireland

United Kingdom

Study participating centre
St. James's University Hospital
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Sponsor information

Organisation
Leeds Teaching Hospitals NHS Trust (UK)

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Research & Development
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Sponsor type
Hospital/treatment centre

Website
http://www.leedsteachinghospitals.com

ROR
https://ror.org/00v4dac24

Funder(s)

Funder type
Industry

Funder Name
Roche

Alternative Name(s)
F. Hoffmann-La Roche Ltd, F. Hoffmann-La Roche & Co, F. Hoffmann-La Roche AG, Roche Holding AG, Roche Holding Ltd, Roche Holding, Roche Holding A.G., Roche Holding, Limited, F. Hoffmann-La Roche & Co.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2017		Yes	No
Plain English results			27/07/2022	No	Yes
HRA research summary			28/06/2023	No	No