ISRCTN88860946 https://doi.org/10.1186/ISRCTN88860946

Single arm NCRI feasibility study of Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone (CHOP) in combination with Ofatumumab in induction and maintenance for patients with newly diagnosed Richters syndrome

Submission date 30/03/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/03/2011	**Overall study status** Completed	
Last Edited 26/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-ofatumumab-with-chop-for-richters-syndrome-chop-or

Study website
http://www.octo-oxford.org.uk/alltrials/trials/CHOP-OR.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2009-016459-23

IRAS number

ClinicalTrials.gov number
NCT01171378

Secondary identifying numbers
9476

Study information

Scientific Title
Single arm NCRI feasibility study of Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone (CHOP) in combination with Ofatumumab in induction and maintenance for patients with newly diagnosed Richters syndrome

Acronym
CHOP-OR

Study objectives
The primary objective of the study will be to evaluate overall response rate (ORR) to CHOP-O (CHOP chemotherapy plus Ofatumumab) according to the Revised Response Criteria for Malignant Lymphoma (Cheson).
Secondary objectives will be feasibility of recruitment, progression free survival and overall survival, the clinical benefit and changes in patient reported outcome measures, safety and tolerability.
This is a multi-centre non-randomised Phase II NCRI feasibility study in 35 patients with newly diagnosed RS in the UK. CHOP-O will be given for six cycles followed by six cycles of Ofatumumab maintenance treatment every eight weeks and a three months follow-up period. The total duration of recruitment will be 24 months starting from the opening of the first site.
Richters Syndrome (RS) is a high-grade transformation that occurs in 5-15% of patients with B cell chronic lymphocytic leukaemia (B-CLL). RS is a complication of B-CLL in which the leukemia changes into a fast-growing diffuse large B cell lymphoma. The pathogenesis of RS is poorly understood and predictors of transformation and response to treatment are unknown. Management of RS remains unsatisfactory; the mean overall survival of patients treated with conventional chemo-immunotherapy such as CHOP-R is 8 months from the end of treatment. CHOP is the acronym for a chemotherapy regimen, cyclophosphamide, hydroxydaunorubicin (doxorubicin), Oncovin (vincristine), and prednisone/prednisolone) and the R stands for the monoclonal antibody, Rituximab. Ofatumumab, a next generation monoclonal anti CD20 antibody, has proven single agent activity in relapsed/refractory B-CLL and other non-Hodgkin lymphomas. In addition, it has shown a favourable safety profile in the maintenance setting. Therefore, the aim of this study is to evaluate Ofatumumab in combination with CHOP in induction and maintenance treatment of patients with RS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
10/H0604/85; First MREC approval date 05/11/2010

Study design
Non-randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Haematological Oncology, Lymphoma; Disease: Leukaemia (chronic), Lymphoma (non-Hodgkin's)

Interventions
CHOP-O (CHOP with Ofatumumab), Subjects will be given CHOP in combination with ofatumumab (CHOP-O).
CHOP-O is CHOP (cyclophosphamide, hydroxydaunorubicin (doxorubicin), Oncovin (vincristine), and prednisone/prednisolone) in combination with the monoclonal antibody, ofatumumab.
The first 4 infusions of CHOP will be weekly. CHOP-O will be given every 3 weeks for six cycles during induction. Subjects will then receive ofatumumab maintenance treatment once every eight weeks for 6 cycles.; Follow Up Length: 3 month(s); Study Entry : Registration only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisone, Ofatumumab

Primary outcome measure
Objective response; Timepoint(s): Objective response as defined by the revised response criteria for malignant lymphoma

Secondary outcome measures
1. To assess feasibility of recruitment
2. To further assess the efficacy of CHOP in combination with ofatumumab in induction and maintenance treatment of Richters Syndrome
3. To assess the safety and tolerability of CHOP in combination with ofatumumab in induction and maintenance treatment of Richters Syndrome

Overall study start date
30/04/2011

Completion date
31/05/2014

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/03/2014:
1. Signed written informed consent prior to performing any study-specific procedures
2. Patients with B-CLL and newly diagnosed not previously treated and biopsy proven Richters transformation - Diffuse large B-cell lymphoma (DLBCL)
3. Computerised tomography (CT) scan performed within 8 weeks prior to starting treatment
4. Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, 2 or 3
5. Age 18 years and over
6. Target gender: male and female
7. Lower age limit 18 years

Previous inclusion criteria:
1. Signed written informed consent prior to performing any study-specific procedures
2. Patients with B-CLL and newly diagnosed not previously treated and biopsy proven Richters transformation - Diffuse large B-cell lymphoma (DLBCL)
3. Computerised tomography (CT) scan performed within 6 weeks prior to starting treatment
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6. Target gender: male and female
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Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 35; UK Sample Size: 35

Total final enrolment
37

Key exclusion criteria
Current exclusion criteria as of 14/03/2014:
1. CHOP or CHOP-like antracycline-containing treatment for DLBCL within 6 months prior to registration
2.Known CNS involvement 1. Treatment for Diffuse large B-cell lymphoma (DLBCL) within 6 months prior to registration
2. Known CNS involvement of B-cell chronic lymphocytic leukemia (B-CLL)
3. Any other malignancy that requires active treatment with the exception of basal cell carcinoma and non-invasive squamous cell carcinoma
4. Chronic or ongoing active infectious disease requiring systemic treatment such as, but not limited to:
4.1. Chronic renal infection
4.2. Chronic chest infection with bronchiectasis
4.3. Tuberculosis
4.4. Active hepatitis
5. Subjects meeting any of the following criteria must not be enrolled in the study:
5.1. Positive serology for Hepatitis B (HB) defined as a positive test for HBsAg. (In addition, if negative for HBsAg but HBcAb positive (regardless of HBsAb status), a HB DNA test will be performed and if positive the subject will be excluded). Consent will be sought prior to any test being performed.
5.2. Clinically significant cardiac disease including:
5.2.1. Unstable angina
5.2.2. Uncontrolled congestive heart failure
5.2.3. Arrhythmia requiring therapy, with the exception of extra systoles or minor conduction abnormalities
5.3. Significant concurrent, uncontrolled medical condition including, but not limited to:
5.3.1. Renal
5.3.2. Hepatic
5.3.3. Haematological
5.3.4. Gastrointestinal
5.3.5. Endocrine
5.3.6. Pulmonary
5.3.7. Neurological
5.3.8. Cerebral or psychiatric disease
5.4. History of significant cerebrovascular disease in last 6 months
5.5. Known HIV positive
6. Known or suspected hypersensitivity to components of investigational product
7. Patients who have received treatment with any non-marketed drug substance or experimental therapy within 4 weeks prior to Visit 2 (start of treatment, cycle 1 day 1)
8. Current participation in any other interventional clinical study
9. Patients known or suspected of not being able to comply with a study protocol (e.g. due to alcoholism, drug dependency or psychological disorder)
10. Breast feeding women or women with a positive pregnancy test at screening.
11. Women of childbearing potential not willing to use adequate contraception during study and for 12 months after last dose of ofatumumab. Adequate contraception is defined as abstinence, hormonal birth control or intrauterine devices

Previous exclusion criteria:
1.Treatment for DLBCL within 6 months prior to registration
2.Known CNS involvement 1. Treatment for Diffuse large B-cell lymphoma (DLBCL) within 6 months prior to registration
2. Known CNS involvement of B-cell chronic lymphocytic leukemia (B-CLL)
3. Any other malignancy that requires active treatment with the exception of basal cell carcinoma and non-invasive squamous cell carcinoma
4. Chronic or ongoing active infectious disease requiring systemic treatment such as, but not limited to:
4.1. Chronic renal infection
4.2. Chronic chest infection with bronchiectasis
4.3. Tuberculosis
4.4. Active hepatitis
5. Subjects meeting any of the following criteria must not be enrolled in the study:
5.1. Positive serology for Hepatitis B (HB) defined as a positive test for HBsAg. (In addition, if negative for HBsAg but HBcAb positive (regardless of HBsAb status), a HB DNA test will be performed and if positive the subject will be excluded). Consent will be sought prior to any test being performed.
5.2. Clinically significant cardiac disease including:
5.2.1. Unstable angina
5.2.2. Congestive heart failure
5.2.3. Arrhythmia requiring therapy, with the exception of extra systoles or minor conduction abnormalities
5.3. Significant concurrent, uncontrolled medical condition including, but not limited to:
5.3.1. Renal
5.3.2. Hepatic
5.3.3. Haematological
5.3.4. Gastrointestinal
5.3.5. Endocrine
5.3.6. Pulmonary
5.3.7. Neurological
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Date of first enrolment
30/04/2011

Date of final enrolment
31/05/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Oxford
Oxford
United Kingdom
OX3 7DQ

Sponsor information

Organisation
University of Oxford

Sponsor details
Clinical Trial & Research Governance Team
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Block 60
Churchill Hospital
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England
United Kingdom
OX3 7LE

Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline (UK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

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
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?
Basic results				No	No
Protocol article	protocol	13/02/2015		Yes	No
Results article	results	01/10/2016	25/04/2019	Yes	No
Plain English results			26/10/2022	No	Yes
HRA research summary			28/06/2023	No	No