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ENRICH Ibrutinib for untreated mantle cell lymphoma

Submission date 21/10/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 21/10/2015	**Overall study status** Ongoing	
Last Edited 23/07/2024	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-ibrutinib-for-older-people-with-mantle-cell-lymphoma-enrich

Study website
https://www.plymouth.ac.uk/penctu/enrich-study

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2015-000832-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19626

Study information

Scientific Title
Randomised, open label study of rituximab/ibrutinib vs rituximab/chemotherapy in older patients with untreated mantle cell lymphoma

Study objectives
The aim of this study is to compare the effect on progression-free survival of treatment with ibrutinib given in combination with rituximab (IR) against treatment with standard chemotherapy given in combination with rituximab.

Ethics approval required
Old ethics approval format

Ethics approval(s)
15/WM/0268

Study design
Multi-centre open-label integrated phase II/III randomised parallel 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 below to request a patient information sheet

Health condition(s) or problem(s) studied
Mantle cell lymphoma (MCL)

Interventions
Current intervention as of 18/04/2023:
Participants are randomly allocated to one of two treatment groups:

Group 1: Participants receive daily ibrutinib in combination with 6 or 8 cycles of rituximab, followed by daily ibrutinib in combination with rituximab maintenance for 2 years, and daily ibrutinib during the follow-up period until disease progression or the end of the study. 126 weeks (2.5 years) of IR however ibrutinib continues until disease progression or end of study.

Group 2: Participants undergo 6-8 cycles of chemotherapy (either CHOP or bendamustine at clinician's discretion) in combination with rituximab, followed by rituximab maintenance for 2 years. No further treatment after the maintenance period. 126 weeks (2.5 years)

Participants in the control arm will be seen every 3-4 weeks during the chemotherapeutic period and every 8 weeks whilst receiving rituximab maintenance. This follow-up will be mirrored exactly for participants in the intervention arm.
In both arms, following the completion of maintenance, participants will be seen every 3 months until disease progression or end of study, as for routine clinical care.

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Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Ibrutinib, rituximab, bendamustine, CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone)

Primary outcome measure
Current primary outcome measure as of 18/04/2023:
Progression-free survival is determined at 2.5 years. This is defined as the interval from the date of randomisation to the earlier of the first documentation of disease progression/relapse or death from any cause.

Previous primary outcome measure:
Progression Free Survival is determined at 2.5 years measured as time from randomisation to first documented evidence of disease progressions or death from any cause.

Secondary outcome measures
Current secondary outcome measures as of 18/04/2023:
1. Overall survival measured as time from randomisation to date of death from any cause is determined at the end of the study
2. Disease response is formally assessed using by CT scans and bone marrow biopsies at baseline, 12 weeks, 24 weeks and every 6 months thereafter until the end of the study
3. Minimal residual disease (MRD) using flow cytometry at end of study
4. Safety and toxicity based on adverse events graded by Common Terminology Criteria for Adverse Event Reporting (CTCAE) v4.03 throughout participation in the study until 30 days post treatment
5. Quality of Life measured using the EORTC QLQ-30 questionnaire at baseline, mid-treatment, end of treatment and end of maintenance
6. Time to next treatment, to include date treatment begins and class of treatment. This will be measured when each participant commences their next treatment regimen, by recording the class of drug that each participant is given as their next line treatment.

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Previous secondary outcome measures:
1. Overall Survival measured as time from randomisation to date of death from any cause is determined at the end of the study
2. Disease response is formally assessed using CT scanning at baseline, 12 weeks, 24 weeks and every 6 months thereafter until the end of the study
3. MRD using flow cytometry at 2.5 years [please expand the abbreviation “MRD”] Minimal Residual Disease
4. Safety and toxicity based on adverse events graded by Common Terminology Criteria for Adverse Event Reporting (CTCAE) v4.03 throughout participation in the study until 30 days post treatment
5. Quality of Life measured using the EORTC QLQ-30 questionnaire at baseline, 12 weeks, 24 weeks and 2.5 years
6. Cost of delivery measured by study-specific worksheets during the treatment period
7. Time to next treatment, to include date treatment begins and class of treatment. This will be

measured when each participant commences their next treatment regimen, by recording the class of drug that each participant is given as their next line treatment.

Overall study start date
01/01/2015

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/04/2023:
1. Male/female patients aged 60 years and over
2. Pathologically confirmed MCL, with documentation of monoclonal B cells that have a chromosome translocation t(11;14)(q13;q32) and/or overexpress cyclin D1
3. Stage II-IV disease, measurable by imaging and requiring treatment in the opinion of the treating clinician
4. No previous treatment for MCL (other than localised radiotherapy or 7-day pulse of steroids for symptom control)
5. Performance status ECOG 0-2
6. Absolute neutrophil count >1.0 x 10(9)/L or platelets >100 x 10(9)/L independent of growth factor support or unless related to lymphoma
7. AST and/or ALT <3xULN
8. Total bilirubin ≤1.5xULN unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin
9. Calculated creatinine clearance >30 mL/min
10. Cardiac function sufficient to tolerate either rituximab-CHOP or rituximab-bendamustine chemotherapy
11. Able to give voluntary written informed consent
12. Willingness and ability to take Pneumocystis jiroveci pneumonia prophylaxis

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8. Total bilirubin ≤1.5xULN unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin
9. Calculated creatinine clearance >30mL/min
10. Cardiac function sufficient to tolerate 300mg/m2 of doxorubicin. A pre-treatment echocardiogram is not mandated, but recommended in patients considered at higher risk of

anthracycline cardiotoxicity
11. Able to give voluntary written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 400; UK Sample Size: 400

Key exclusion criteria
Current exclusion criteria as of 18/04/2023:
1. Patients considered fit enough to undergo autologous or allogeneic stem cell transplant as treatment for MCL
2. Known serological positivity for HBV, HCV, HIV
3. Vaccinated with live vaccines within 4 weeks prior to Day 1 of Cycle 1
4. Major surgery within 2 weeks prior to Day 1 of Cycle 1
5. Diagnosed with or treated for any other malignancy than MCL within 2 years prior to Day 1 of Cycle 1 (except BCC, SCC or any in situ malignancy)
6. Active systemic infection requiring treatment
7. Male subjects with female partners of childbearing potential who are unwilling to use appropriate contraception methods whilst on study treatment
8. Women who are pregnant or breastfeeding
9. Serious medical or psychiatric illness likely to interfere with participation in this clinical study
10. Concurrent treatment with another investigational agent
11. CNS involvement of MCL

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6. Active systemic infection requiring treatment
7. Male subjects with female partners of childbearing potential who are unwilling to use appropriate contraception methods whilst on study treatment (see section 8.4)
8. Women who are pregnant or breastfeeding
9. Serious medical or psychiatric illness likely to interfere with participation in this clinical study
10. Concurrent treatment with another investigational agent

Date of first enrolment
24/11/2015

Date of final enrolment
30/06/2021

Locations

Countries of recruitment
Denmark

England

Finland

Norway

Sweden

United Kingdom

Study participating centre
Derriford Hospital (lead hospital)
Derriford Road
Plymouth
United Kingdom
PL6 8DH

Sponsor information

Organisation
University Hospitals Plymouth NHS Trust

Sponsor details
Research Office
Level 2 MSCP, Bircham Park Offices
1 Roscoff Rise
Derriford
Plymouth
England
United Kingdom
PL6 5FP
+44 (0)1752 432842
plh-tr.RD-Office@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.plymouthhospitals.nhs.uk/home

ROR
https://ror.org/05x3jck08

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

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
It is likely that the results, analysis and discussion will be published in an appropriate high impact haematology specialist journal. Poster or platform presentations may be made at regional, national or international conferences as appropriate. The TMG will prepare a plain English summary of the study results which will be posted on the website www.mantlecelllymphoma.org.uk

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from penctudata@plymouth.ac.uk. The data will be made available after publication.

IPD sharing plan summary

Available on request

Study outputs

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