

ENRICH Ibrutinib for untreated mantle cell lymphoma

Submission date 21/10/2015	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 21/10/2015	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 23/07/2024	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

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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Scientific

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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.

Previous intervention:

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 two 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.

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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.

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 $>1.0 \times 10^9/L$ or platelets $>100 \times 10^9/L$ independent of growth factor support or unless related to lymphoma
7. AST and/or ALT $<3 \times \text{ULN}$
8. Total bilirubin $\leq 1.5 \times \text{ULN}$ unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin
9. Calculated creatinine clearance $>30 \text{ mL/min}$
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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7. AST and/or ALT $<3 \times \text{ULN}$
8. Total bilirubin $\leq 1.5 \times \text{ULN}$ unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin
9. Calculated creatinine clearance $>30 \text{ mL/min}$
10. Cardiac function sufficient to tolerate 300 mg/m^2 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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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 (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