

# ENRICH Ibrutinib for untreated mantle cell lymphoma

<b>Submission date</b> 21/10/2015	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 21/10/2015	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/10/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input checked="" 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

### Contact name

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### Contact details

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Scientific

### Contact name

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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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Previous intervention:

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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  $>1.0 \times 10^9/L$  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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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  $300 \text{ mg/m}^2$  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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4. Major surgery within two 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 (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**

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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, Cancer Research UK (CRUK), 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](http://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](mailto: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?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			21/10/2025	No	Yes