

# A trial of zanubrutinib treatment of patients with relapsed and refractory primary central nervous system lymphoma

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<b>Registration date</b> 25/03/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 17/12/2025	<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

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-zanubrutinib-for-lymphoma-of-the-brain-and-spinal-cord-prizm>

### Background and study aims

Primary central nervous system lymphoma (PCNSL) is a rare type of brain tumour. It is an aggressive type of non-Hodgkin lymphoma that is found only in the brain or spinal cord. PCNSL is often treated with high doses of chemotherapy. The first treatment doesn't work for some patients (called 'refractory'), and the lymphoma can come back (called 'relapse'). Refractory or relapsed (RR) PCNSL is much more difficult to treat. There is currently no standard treatment for RR-PCNSL and further chemotherapy treatment is often unsuccessful. Radiation treatment to the brain can sometimes be used but can cause significant long-term side effects.

Clinical trials are now focused on testing new drugs that are better at targeting the tumour and are likely to have fewer side effects. The treatment being tested in this study is a drug called zanubrutinib. Zanubrutinib is a new type of drug (a Bruton's tyrosine kinase inhibitor), which works by targeting lymphoma cells. Previous studies have shown that similar drugs can cause RR-PCNSL to shrink or disappear. It is thought that zanubrutinib could be a more effective treatment that can be given safely without too many side effects. The aim of the study is to find out how effective and safe zanubrutinib is for patients with RR-PCNSL. The researchers will be looking at the effects zanubrutinib has against lymphoma, how long these effects last, and what the side effects of the drug are.

### Who can participate?

Patients who have not responded to standard chemotherapy for PCNSL or have relapsed afterwards. Patients with this type of brain tumour often have impaired cognitive function due to their disease and previous therapy, but this has been known to improve in patients who respond well to treatment, so these patients are included in this trial.

### What does the study involve?

Participants will receive 28-day cycles of continuous zanubrutinib treatment orally twice daily. The participants will continue until disease progression, development of unacceptable side

effects, or their choice. Participants no longer on treatment will be followed up every 3 months for survival, progression and subsequent treatment.

What are the possible risks and benefits of participating?

There is always a risk associated with taking any drug. There may be risks of the study drug that are unknown or cannot be predicted at this time, but patients will be carefully monitored for any problems or adverse side effects. The treatments may or may not improve patients' underlying disease.

Where is the study run from?

University of Birmingham and the Cancer Research UK Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?

April 2019 to December 2028

Who is funding the study?

Beigene (China) and Cure Leukaemia (UK)

Who is the main contact?

Emma Homer (trial coordinator)

PRiZM+@trials.bham.ac.uk

## Contact information

### Type(s)

Principal investigator

### Contact name

Prof Chris Fox

### Contact details

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### Type(s)

Scientific

### Contact name

Dr Emma Homer

### Contact details

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Institute of Cancer and Genomic Sciences  
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## Additional identifiers

### Clinical Trials Information System (CTIS)

2020-005218-16

### Integrated Research Application System (IRAS)

290665

### Central Portfolio Management System (CPMS)

50538

## Study information

### Scientific Title

PRiZM+: a Phase II platform study of zanubrutinib monotherapy and combination therapy for relapsed and refractory primary central nervous system lymphoma

### Acronym

PRiZM+

### Study objectives

Is zanubrutinib (a new drug that interferes with signals that B cells need to survive and grow) a safe and effective treatment for patients with an aggressive brain tumour known as primary central nervous system lymphoma (PCNSL), who have either not responded to initial chemotherapy, or have relapsed after chemotherapy?

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Approved 05/11/2021, East Midlands – Leicester Central REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 104 8115; leicestercentral.rec@hra.nhs.uk), ref: 21/EM/0224

### Study design

Non-randomized; Interventional; Design type: Treatment, Drug

### Primary study design

Interventional

### Study type(s)

Treatment

### Health condition(s) or problem(s) studied

## Relapsed and refractory primary CNS lymphoma

### **Interventions**

This is a prospective, multicentre, sequential single-arm phase II study for zanubrutinib for the treatment of RR-PCNSL.

Patients and legal representatives who consent to participate will have a screening period of up to 28 days before trial registration for the following assessments to take place. The patient will be asked their demographic and medical history, physical exam (including vital signs, height and weight), pregnancy test (for women of childbearing potential [WOCBP]), blood tests, lumbar puncture and cerebrospinal fluid (CSF) evaluation, Eastern Cooperative Oncology Group (ECOG) performance status, Neurologic Assessment for Neuro-Oncology (NANO), functional assessment, ophthalmological slit lamp exam, MRI scan and a PET-CT scan (or CT-NCAP [neck-chest-abdomen-pelvis]).

Once registered to the study, patients will receive 28-day cycles of continuous zanubrutinib monotherapy orally twice daily. The patient will continue until disease progression, development of unacceptable side effects, or patient choice.

Patients will be seen on day 1 of cycle 1 for vital signs, physical exam, pregnancy test (for WOCBP), blood tests, ECOG performance status and NANO. Days 7 and 14 of cycle 1 they will be seen again for blood tests, lumbar puncture and CSF evaluation and an ECOG performance status. Day 1 of cycle 2 the patient will be seen for vital signs, blood tests, lumbar puncture and CSF evaluation, ECOG performance status and a multimodal MRI scan. On day 1 of cycle 3 the patient will be seen for the same assessments as mentioned for cycle 2, but also a physical exam, NANO, functional assessment, ophthalmological slit lamp exam and a Gd-enhanced MRI. Following cycle 3, patients will be seen on day 1 of each cycle for vital signs, blood tests and ECOG performance status assessment. Every 3 months during treatment the patient will be seen for a NANO, functional assessment and Gd-enhanced MRI. Every 6 months they will be seen for an additional blood test for circulating tumour DNA.

If the patient experiences disease progression, they will be seen for vital signs, blood tests, ECOG performance status, NANO and functional assessment. They will be seen 28 days after the last dose of trial treatment for an End of Treatment visit, this will include vital signs, blood tests, ECOG performance status, NANO and Gd-enhanced MRI.

Patients no longer on treatment will be followed up every 3 months for survival, progression date and subsequent therapy.

### **Intervention Type**

Drug

### **Phase**

Phase II

### **Drug/device/biological/vaccine name(s)**

Zanubrutinib

### **Primary outcome(s)**

Overall response (complete response [CR] + unconfirmed CR [CRu] + partial response [PR]) after two cycles of treatment, assessed locally using international consensus criteria (Abrey et al., 2005). Patients will be followed up for 1 year.

### **Key secondary outcome(s)**

Patients will be followed up for 1 year:

1. Complete response at response assessment by MRI scan after two cycles of treatment, response assessed locally or by central MRI scan review
2. Overall response assessed by MRI scan after two cycles of treatment, assessment by central MRI review
3. Best overall response assessed by MRI scan within 12 months of registration, response assessed locally or by central MRI scan review
4. Progression-free survival, defined as the time from trial entry to the date of progressive disease or death from any cause
5. Overall survival, defined as the time from trial entry to the date of death from any cause
6. Event-free survival, defined as the time from trial entry to the first of initiation of a new anti-lymphoma treatment, progressive disease, or death from any cause
7. Toxicity, defined as the proportion of patients experiencing one or more: grade 2 or higher non-haematological adverse events (AE), grade 3 or higher haematological AE, or any serious AE (SAE)

### **Completion date**

31/12/2028

## **Eligibility**

### **Key inclusion criteria**

1. Aged  $\geq 16$  years of age
2. Histologically confirmed CD20+ diffuse large B cell lymphoma (DLBCL) confined to the CNS
3. Relapsed or refractory PCNSL (defined as disease progression following complete response (CR)/unconfirmed complete response (CRu)/partial response (PR), or failure to achieve PR after one or more lines of therapy; one therapy line must have included at least 1 cycle of high-dose methotrexate [ $\geq 1$  g/m<sup>2</sup>])
4. Measurable disease on contrast-enhanced MRI of brain (and/or spinal cord)
5. ECOG performance status of 0 to 2, or 3 if attributed to lymphoma
6. Ability to swallow capsules
7. Adequate renal and liver function defined as:
  - 7.1. Creatinine clearance  $\geq 30$  ml/min (as estimated by the Cockcroft-Gault equation or as measured by nuclear medicine scan or 24-hour urine collection)
  - 7.2. Serum total bilirubin  $< 3.0 \times$  ULN (unless due to Gilbert's syndrome)
  - 7.3. Up to and including moderate impairment (Child-Pugh class B)
8. Adequate bone marrow function, defined as unsupported platelets  $> 50 \times 10^9/l$ , neutrophils  $> 1 \times 10^9/l$ , haemoglobin  $> 80$  g/l
9. Patient willing and able to comply with scheduled visits, treatment plan, investigations and other study procedures
10. Written informed consent for the trial

### **Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

16 years

**Upper age limit**

99 years

**Sex**

All

**Total final enrolment**

0

**Key exclusion criteria**

1. Current evidence or prior history of systemic lymphoma
2. Exclusive intraocular involvement
3. Active infection requiring intravenous antimicrobials
4. Chemotherapy for lymphoma within 2 weeks of the first dose of zanubrutinib
5. Whole-brain radiotherapy within 4 weeks of the first dose of zanubrutinib
6. Contra-indication to lumbar puncture
7. Prior exposure to BTK inhibitor
8. Known bleeding disorder e.g haemophilia or severe Von-Willebrand Disease
9. Current use of warfarin, or dual anti-platelet therapy. Therapeutic anticoagulation with direct oral anticoagulants or low molecular weight heparin is permitted
10. Evidence of active HIV, HBV or HCV infection, except:
  - 10.1. HIV-positive patients established on anti-retroviral treatment, with undetectable HIV RNA, after discussion with the patient's HIV physician
  - 10.2. HBV core antibody-positive patients who are (i) surface antigen-negative and (ii) HBV DNA PCR negative, who take prophylaxis as per institutional guidelines
11. Patients who are pregnant or breastfeeding (women of childbearing potential must have a negative urine or serum pregnancy test prior to trial entry)
12. Patients and patients with partners of childbearing potential (pre-menopausal female capable of becoming pregnant) not willing to use highly effective contraception (see Section 9.6) during and for 12 months after cessation of therapy
13. Clinically significant cardiac or respiratory dysfunction that, in the opinion of the investigator, would jeopardise the safety of the patient in the trial
14. Active malignancy treated in the last 2 years, except:
  - 14.1. Non-melanoma skin cancer
  - 14.2. Carcinoma in situ of the cervix or breast
  - 14.3. Incidental finding of prostate cancer (T1a or T1b)

**Date of first enrolment**

20/10/2022

**Date of final enrolment**

31/07/2027

# Locations

## Countries of recruitment

United Kingdom

England

Northern Ireland

Scotland

Wales

## Study participating centre

### **Aberdeen Royal Infirmary**

Foresterhill Road

Aberdeen

Scotland

AB25 2ZN

## Study participating centre

### **Churchill Hospital**

Churchill Hospital

Old Road

Headington

Oxford

England

OX3 7LE

## Study participating centre

### **Beatson West of Scotland Cancer Centre**

1053 Great Western Road

Glasgow

Scotland

G12 0YN

## Study participating centre

### **Belfast City Hospital**

51 Lisburn Rd

Belfast

Northern Ireland

BT9 7AB

**Study participating centre**  
**Clatterbridge Cancer Centre**  
65 Pembroke PLACE  
Liverpool  
England  
L7 8YA

**Study participating centre**  
**Christie Hospital**  
Wilmslow Road  
Manchester  
England  
M20 4BX

**Study participating centre**  
**King's College Hospital**  
Denmark Hill  
London  
England  
SE5 9RS

**Study participating centre**  
**Freeman Road Hospital**  
Freeman Road  
High Heaton  
Newcastle upon Tyne  
England  
NE7 7DN

**Study participating centre**  
**Nottingham University Hospital**  
Queens Medical Centre  
Derby Road  
Nottingham  
England  
NG7 2UH

**Study participating centre**

**Royal Hallamshire Hospital**

Glossop Road  
Sheffield  
England  
S10 2JF

**Study participating centre**

**Southampton General Hospital**

Tremona Road  
Southampton  
England  
SO16 6YD

**Study participating centre**

**St. Bartholomews Hospital**

West Smithfield  
London  
England  
EC1A 7BE

**Study participating centre**

**St James's University Hospital**

Beckett Street  
Leeds  
England  
LS9 7TF

**Study participating centre**

**University Hospital Birmingham**

Queen Elizabeth Hospital  
Edgbaston  
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B15 2TH

**Study participating centre**

**University College London Hospital**

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London  
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NW1 2BU

**Study participating centre**  
**University Hospital of Wales**  
Heath Park  
Cardiff  
Wales  
CF14 4XW

## Sponsor information

**Organisation**  
University of Birmingham

**ROR**  
<https://ror.org/03angcq70>

## Funder(s)

**Funder type**  
Charity

**Funder Name**  
Cure Leukaemia

**Funder Name**  
BeiGene

**Alternative Name(s)**  
, BeiGene Ltd, BeiGene, Ltd.

**Funding Body Type**  
Government organisation

**Funding Body Subtype**  
For-profit companies (industry)

**Location**  
China

# Results and Publications

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No