

# Investigating the most appropriate dose and effectiveness of thiotepa in combination with ifosphamide, etoposide and rituximab in patients with lymphoma arising in the brain or spinal cord

<b>Submission date</b> 03/12/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 03/12/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 15/02/2023	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-chemotherapy-and-biological-therapy-for-lymphoma-of-the-brain-or-spinal-cord-tier>

## Contact information

### Type(s)

Scientific

### Contact name

Ms Louise Hopkins

### Contact details

Cancer Research UK Clinical Trials Unit  
School of Cancer Sciences  
University of Birmingham  
Edgbaston  
Birmingham  
United Kingdom  
B15 2TT

## Additional identifiers

### Clinical Trials Information System (CTIS)

2014-000227-24

**Protocol serial number**

17668

## Study information

**Scientific Title**

A study of thiotepa, ifosphamide, etoposide and rituximab for the treatment of relapsed or refractory primary central nervous system lymphoma

**Acronym**

TIER

**Study objectives**

The phase I dose finding component is a 3+3 cohort design which will recruit up to 18 patients in order to find the MTD of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER). All patients recruited into phase I at the MTD will also contribute towards phase II. The phase II study is based on an A'Hern's design to assess the activity of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER). 28 patients will be recruited in total in phase II (including some patients from phase I).

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

14/LO/1568; First MREC approval date

**Study design**

Non-randomised, interventional

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Primary central nervous system lymphoma

**Interventions**

Etoposide, 250mg/m<sup>2</sup> day 2 of 21 day cycle; Ifosphamide, 2g/m<sup>2</sup>/day days 2-4 for each 21 day cycle.; Rituximab, 375mg/m<sup>2</sup>/day days 1-2 for each 21 day cycle; Thiotepa, Chemotherapy (doses 20mg/m<sup>2</sup> - 50mg/m<sup>2</sup>)

**Intervention Type**

Drug

**Phase**

Phase I/II

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

1. Etoposide 2. Ifosphamide 3. Rituximab 4. Thiotepa

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

MTD of thiotepa in combination with ifosphamide, etoposide and rituximab (TIER)

Timepoint(s): End of 2 cycles of treatment

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

1. 2 year event free survival (EFS); Timepoint(s): 2 years after trial treatment
2. 2 year overall survival (OS); Timepoint(s): 2 years after trial treatment
3. 2 year progression free survival (PFS); Timepoint(s): 2 years after trial treatment
4. CR rate after 2 cycles of TIER; Timepoint(s): End of 2 cycles of treatment
5. Overall response rate (Complete Response (CR) + Complete Response: unconfirmed (CRu) + Partial Res; Timepoint(s): end of 2 cycles of treatment
6. Proportion of patients proceeding to high-dose therapy and autologous stem cell transplant (HDT-AS; Timepoint(s): Following trial treatment
7. Rate of successful stem cell harvest; Timepoint(s): After completing trial treatment
8. Toxicity of TIER using the National Cancer Institute Common Terminology Criteria for Adverse Event; Timepoint(s): All cycles of trial treatment

### **Completion date**

31/10/2021

## **Eligibility**

### **Key inclusion criteria**

- 1 Age  $\geq$  16 years of age
2. Histologically confirmed\* CD20+ Diffuse Large B Cell Lymphoma (DLBCL) confined to the central nervous system
3. Relapsed or refractory primary central nervous system lymphoma (PCNSL) according to the following definition :
  - 3.1. One or two prior chemotherapy regimen(s), of which at least one regimen contained highdose methotrexate at a dose of  $>1\text{g}/\text{m}^2$ .
  - 3.2. Minimum of one cycle containing highdose methotrexate
4. ECOG performance status 0,1 or 2 (or 3 if attributed to lymphoma)
5. Adequate organ function:
  - 5.1. Bone marrow: platelets  $>80 \times 10^9/\text{L}$ , neutrophils  $>1 \times 10^9/\text{L}$ , haemoglobin  $>80 \text{g}/\text{L}$
  - 5.2. Hepatic: bilirubin  $<1.5 \times$  upper limit of normal (ULN) (unless isolated unconjugated hyperbilirubinaemia attributable to Gilbert's syndrome)
  - 5.3. Renal: eGFR  $\geq 40\text{ml}/\text{min}$  (Cockcroft-Gault)
  - 5.4. Cardiorespiratory (as judged by the Local Investigator): clinically relevant cardiac or pulmonary function tests must be performed if there is a previous history of significant cardiac or pulmonary impairment
6. Able to comply with the scanning requirements of the study
7. Valid Informed consent

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

Patient

### **Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Total final enrolment**

36

**Key exclusion criteria**

1. Systemic involvement with lymphoma
2. Active infection requiring intravenous antimicrobials
3. Chemotherapy for lymphoma within 4 weeks registration
4. Wholebrain radiotherapy within 6 months of registration
5. Relapse within 1 year of a Thiotepabased autologous stem cell transplant
6. Prior therapy with the RIE (Rituximab – ifosphamide and etoposide) regimen
7. Evidence of HIV or Hepatitis C infection
8. Hepatitis B infection\*
9. Serum albumin <25g/l
10. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry)
11. Competent pPatients and competent patients with partners of childbearing potential not willing to use effective contraception during and for 12 months after therapy

**Date of first enrolment**

12/12/2014

**Date of final enrolment**

30/04/2019

**Locations****Countries of recruitment**

United Kingdom

England

Scotland

**Study participating centre**

**Cancer Research UK Clinical Trials Unit**

School of Cancer Sciences

University of Birmingham

Edgbaston

Birmingham

United Kingdom

B15 2TT

**Study participating centre**  
**Queen Elizabeth Hospital**  
Mindelsohn Way  
Birmingham  
United Kingdom  
B15 2TH

**Study participating centre**  
**Aberdeen Royal Infirmary**  
Aberdeen  
United Kingdom  
AB25 2ZN

**Study participating centre**  
**Beatson West of Scotland Cancer Centre**  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**  
**King's College Hospital**  
London  
United Kingdom  
SE5 9RS

**Study participating centre**  
**St James University Hospital**  
Leeds  
United Kingdom  
LS9 7TF

**Study participating centre**  
**Aintree University Hospital**  
Liverpool  
United Kingdom  
L9 7AL

**Study participating centre**  
**The Christie**  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**  
**Freeman Hospital**  
Newcastle  
United Kingdom  
NE7 7DN

**Study participating centre**  
**Nottingham City Hospital**  
Nottingham  
United Kingdom  
NG5 1PB

**Study participating centre**  
**Churchill Hospital**  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**  
**Derriford Hospital**  
Plymouth  
United Kingdom  
PL6 8DH

**Study participating centre**  
**University College Hospital**  
London  
United Kingdom  
NW1 2BU

**Study participating centre**  
**The Royal Marsden Hospital**  
Sutton

United Kingdom  
SM2 5PT

**Study participating centre**  
**Royal Hallamshire Hospital**  
Sheffield  
United Kingdom  
S10 2JF

**Study participating centre**  
**Southampton General Hospital**  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**New Cross Hospital**  
Wolverhampton  
United Kingdom  
WV10 0QP

## **Sponsor information**

**Organisation**  
University of Birmingham

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

## **Funder(s)**

**Funder type**  
Government

**Funder Name**  
Leukaemia and Lymphoma Research

**Alternative Name(s)**

## Funding Body Type

Private sector organisation

## Funding Body Subtype

Other non-profit organizations

## Location

United Kingdom

# Results and Publications

## 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?
<a href="#">Results article</a>		26/10/2021	15/02/2023	Yes	No
<a href="#">Basic results</a>		15/02/2023	15/02/2023	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			25/10/2022	No	Yes