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Risk-adapted treatment for cancer of the immune system

Submission date 07/07/2026	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 06/10/2026	**Overall study status** Ongoing	
Last Edited 06/11/2026	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

Large B-cell Lymphoma refers to a group of aggressive B cell lymphomas including diffuse Large B-cell Lymphoma (DLBCL) and high-grade B cell lymphoma. Approximately 1 in 3 patients' lymphoma will either fail to respond (r) to treatment or relapse (r) after an initial response. Current standard treatments for patients are R-CHOP and Pola-R-CHP. Currently available tools are unable to accurately predict which patients are at highest risk of failing to respond or relapsing (r/r).

The RAdICAL trial aims to find out whether new scientific tools can more accurately identify patients at highest risk of r/r LBCL. The trial will use 4 different tests to do this using extra blood tests, diagnostic tissue biopsy material and PET scans. Participants found to be high-risk from one or more of these tests will receive an additional drug, called Epcoritamab, as well as the standard of care R-CHOP/Pola-RCHP. Participants found to be not high-risk will receive R-CHOP /Pola-RCHP only.

Who can participate?

Patients aged 18-80 years, with Large B-cell lymphoma.

What does the study involve?

All participants will receive one initial cycle of R-CHOP/Pola-RCHP, during which it will be determined if they are in the high-risk group. Participants determined to be non high-risk will receive treatment every 3 weeks, for 6 cycles in total. Participants in the high-risk group will attend for the same treatment but will also receive Epcoritamab and 2 additional doses of of Epcoritamab after cycle 6. Participants will have blood tests and an examination to make sure they are well enough to receive treatment. Participants will have up to 3 PET scans, a CT scan and be followed up for 24 months.

What are the possible benefits and risks of participating?

Clinical trials are carefully designed to reduce the risks and increase the benefits to all participants. However, we cannot guarantee that participants will have any specific treatment benefits when taking part in a trial. We also cannot guarantee to participants that there are no risks involved when taking part in a trial.

Possible benefits:

· The trial treatment may improve the chance of your lymphoma going into remission and increase the chance of staying in remission.
· You will be helping to further our knowledge of how to treat cancer and this will benefit society and others with the same condition in the future
Possible risks/disadvantages:
· The trial treatment may not provide additional benefit to standard treatment
· There may be additional risks or side effects (further information can be found in the Patient Information Sheet)
· You will need to attend more clinic visits, provide more blood samples and have some additional scans than if you were not taking part in the trial.
· There could be risks to your child if you, or your partner, become pregnant, or begin breastfeeding (further information can be found in the Patient Information Sheet)

Where is the study run from?
University of Southampton (UK)

When is the study starting and how long is it expected to run for?
September 2026 to June 2030

Who is funding the study?
Genmab (Denmark)
AbbVie (USA)

Who is the main contact?
radical@soton.ac.uk

Contact information

Type(s)
Scientific

Contact name
None - RAdICAL Trial Team

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Integrated Research Application System (IRAS)
1009922

Central Portfolio Management System (CPMS)
61653

Sponsor's protocol code number
107447

Study information

Scientific Title
RAdICAL: Risk-Adapted Immunochemotherapy to Cure Aggressive Lymphoma

Acronym
RAdICAL

Study objectives
Primary objectives:
1. To determine the proportion of participants with newly diagnosed LBCL who are identified as high-risk of refractory or relapsed disease, based on the presence of any of the following 4 pre-treatment risk factors:
1.1. 'Molecular high-grade' (MHG) signature on gene expression profiling and/or
1.2. High baseline plasma ctDNA (defined as a tumour fraction of ≥0.11) and/or
1.3. Presence of pathogenic TP53 mutation(s) and/or
1.4. High-risk IMPI score (IMPI is based on PET MTV, age and stage
2. To evaluate the efficacy in terms of progression-free survival of adding epcoritamab to standard of care first-line therapy for LBCL participants at high-risk of refractory or relapsed disease

Secondary objectives:
1. To assess the concordance of the pre-treatment risk factors
2. To evaluate treatment duration and relative dose intensity of epcoritamab-treated participants
3. To assess response rates in epcoritamab-treated participants
4. To summarise event-free survival in epcoritamab-treated participants and separately in non-high-risk participants (not treated with epcoritamab)
5. To summarise overall survival in epcoritamab-treated participants and separately in non-high-risk participants (not treated with epcoritamab)
6. To summarise progression-free survival in non-high-risk participants (not treated with epcoritamab)

7. To summarise the serious adverse events and adverse events in epocoritamab-treated participants

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 07/07/2026, to be confirmed (-, -, -, United Kingdom; -; -), ref: 26/SC/0245

Primary study design
Interventional

Allocation
Non-randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Large B-cell lymphoma

Interventions
All participants will receive one initial cycle of R-CHOP/Pola-RCHP as per International Prognostic Index (IPI)-guided Standard of Care (Rituximab 375 mg/m², Cyclophosphamide 750 mg /m², Vincristine 1.4mg m² (max 2mg) or Polatuzumab vedotin 1.8mg/kg, Doxorubicin 50 mg/m²; i. v and prednisolone 100mg OD, oral.)
In parallel a panel of known risk factors will be assessed to see if the participant is considered high-risk or non high risk of refractory or relapsed LBCL (rrLBCL). Local research teams will be informed of the risk assignation for each participant by Southampton Clinical Trials Unit based on the results from the assessment of risk factors.

Participants determined to be non high-risk will continue to receive R-CHOP/Pola-RCHP treatment every 3 weeks, for 6 cycles in total.
Participants in the high-risk group will attend for the same treatment but will also receive Epcoritamab and 2 additional doses of Epcoritamab after cycle 6. Epcoritamab will be administered weekly via subcutaneous (SC) injection according to a step up dose schedule with a dose range of 0.16mg (step-up dose 1), 0.8mg (step-up dose 2) and 48mg (full dose).

Participants will have blood tests and an examination to make sure they are well enough to receive treatment. Participants will have up to 3 PET scans, a CT scan and be followed up for 24 months.

Duration of treatment per participant: All cycles will be 21-day cycles
Non High Risk Arm: 18 weeks
High Risk Arm: 24 weeks

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Tepkinly [epcoritamab], MabThera [rituximab], cyclophosphamide, doxorubicin, vincristine, prednisolone, polatuzumab vedotin

Primary outcome(s)
Joint primary outcomes:
1. The proportion of participants with newly diagnosed LBCL who are identified as high-risk of refractory or relapsed disease, based on the 4 pre-treatment risk factors measured using the clinical trial data set at the start of cycle 2
2. The efficacy in terms of progression-free survival of adding epcoritamab to IPI derived SoC in first-line therapy in LBCL participants at high-risk of refractory or relapsed disease measured using the Response Assessment by Lugano Classification
at the end of 2 year follow up

Key secondary outcome(s)
1. Number of participants identified as high-risk by the individual pre-treatment risk factors and the degree of concordance between these 4 risk factors measured using the clinical trial data set at the start of cycle 2
2. Relative dose intensity (RDI) of SOC therapy + epcoritamab measured using the clinical trial data set at the end of cycle 8
3. Complete metabolic response rate measured using response assessment by Lugano Classification at the end of treatment
4. Overall response rate measured using response assessment by Lugano Classification at the end of 2 year follow up
5. Event free survival of high-risk and non high-risk participants measured using the clinical trial data set at the end of 2 year follow up
6. Overall survival of high-risk and non high-risk participants measured using the clinical trial data set at the end of 2 year follow up
7. Number of participants receiving a new anti-lymphoma therapy measured using the clinical trial data set at the end of 2 year follow up
8. Progression free survival of non high-risk participants measured using the clinical trial data set at the end of 2 year follow up
9. Toxicity, including serious adverse events, adverse events and epcoritamab adverse events of special interest according to CTCAE version 5.0 and coded using MedDRA, measured using the clinical trial data set at the end of 2 year follow up

Completion date

01/06/2030

Eligibility

Key inclusion criteria

1. Histologically confirmed LBCL, expressing CD20. Sufficient diagnostic material must be available to send to HMDS for gene expression profiling and central pathology review. The following diagnoses by the 2016 WHO classification of lymphoid neoplasms may be included:
1.1. DLBCL, not otherwise specified (NOS)
1.2. T-cell/histiocyte-rich large B-cell lymphoma
1.3. High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (double-hit or triple-hit lymphoma)
1.4. High-grade B-cell lymphoma, NOS
1.5. LBCL arising from underlying indolent lymphoma (marginal zone or follicular sub-types) where the indolent lymphoma has been exclusively under observation and not previously treated
2. FDG-avid assessable disease
3. Not previously treated for lymphoma and intended for treatment with 6 cycles of RCHOP /Pola-RCHP with curative intent
4. Participants must have an ECOG performance status of 0-2 prior to initiating treatment. Participants with an ECOG ≥3 may be screened if pre-phase treatment is planned. Subject may be eligible if ECOG performance status were to improve to 0-2 after pre-phase treatment.
5. Haemoglobin ≥8.0 g/dL (red cell transfusion permitted)
6. Adequate bone marrow function with platelets >75x10^9/L; neutrophils >1.0x10^9/L at study entry
7. Measured or calculated creatinine clearance > 40mls/min, (calculated using the formula of Cockcroft and Gault [(140-Age) x Mass (kg) x (1.04 (for women) or 1.23 (for men))/Serum Creatinine (µmolL)])
8. Serum bilirubin <1.5 x the upper limit of normal and transaminases <2.5 x the upper limit of normal at the time of study entry
9. Cardiac function sufficient to tolerate 300mg/m² of doxorubicin
a. No formal assessment of LVEF function is required if the 12-lead ECG is normal and there is no cardiac history
b. If the 12-lead ECG is not normal or there is a history of cardiac morbidity, a pre-treatment echocardiogram or MUGA is required to establish a baseline ≥50% LVEF equal to or greater than the institutional normal range
10. No concurrent uncontrolled medical condition that would preclude treatment with R-CHOP /Pola-RCHP
11. Aged ≥ 18 years old and < 80 years old
12. Ability to understand the purpose and risks of the study and provide signed and dated informed consent

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

18 Years

Upper age limit

80 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Participants who have received immunisation with a live vaccine within four weeks prior to enrolment will be ineligible
2. Diagnosis of primary mediastinal lymphoma
3. Diagnosis of primary Central Nervous System lymphoma or secondary CNS involvement. Those participants presenting with neurological symptoms should be investigated for CNS involvement. Routine CNS imaging or diagnostic lumbar puncture will not be required in the absence of symptoms
4. Seizure disorder requiring anti-epileptic therapy unless well-controlled and seizure-free for >12 months
5. Active significant infection (e.g. progressive multifocal leukoencephalopathy (PML), tuberculosis, sepsis, and opportunistic infections)
6. Uncontrolled autoimmune haemolytic anaemia (AIHA) or idiopathic thrombocytopenic purpura (ITP)
7. Participants with pre-existing peripheral neuropathy ≥ grade 2
8. Major surgery in the 2 weeks prior to enrolment. If a participant has undergone recent major surgery >2 weeks ago, they must have recovered adequately from the surgery and any complications before the first dose of Epcoritamab
9. Corticosteroid use >10 mg day of prednisolone or equivalent, for purposes other than lymphoma symptom control
If glucocorticoid treatment is urgently required for lymphoma symptom control prior to the start of study treatment, prednisone 100 mg or equivalent could be given for a maximum of 72 hours prior to PET scan and ctDNA collection
10. No clinically significant cardiovascular disease, including:
10.1. Myocardial infarction or stroke within 6 months prior to study entry
10.2. Unstable or uncontrolled disease/condition related to or affecting cardiac function (e.g. unstable angina, congestive heart failure, New York Heart Association Class III-IV), uncontrolled cardiac arrhythmia within the last 3 months
10.3. Screening 12-lead ECG showing a baseline QT interval as corrected by Fredericia's formula (QTcF) >470 msec (Male) or >480 msec (female)
10.4. Other clinically significant ECG abnormalities within 6 months prior to enrolment unless deemed stable and appropriately treated
11. Participants with a history of treatment for tuberculosis (TB) in the past 12 months and participants with latent TB must initiate treatment for latent TB before enrolment into the study
12. Serological positivity for Hepatitis B, C, or known HIV infection. As per standard of care, prior to initiation of immunochemotherapy, the results of hepatitis serology should be known prior to commencement of therapy.
12.1. Positive test results for chronic HBV infection (defined as positive HBsAg serology) will not be eligible. Participants with occult or prior HBV infection (defined as negative HBsAg and positive total HBcAb) may be included if HBV DNA is negative, if they are willing to undergo HBV DNA PCR testing, and prescribed HBV prophylaxis. Participants who have protective titres of hepatitis B surface antibody (HBsAb) after vaccination will be eligible.
12.2. Participants positive for HCV antibody are eligible only if polymerase chain reaction (PCR)

is negative for HCV RNA.
13. Women who can bear children must agree to use one highly effective form of contraception with an additional barrier or abstinence during the study and for 12 months after the last treatment dose.
14. Breastfeeding or pregnant women
15. Men who can father children must agree to use one highly effective form of contraception with an additional barrier or abstinence during the study and for 12 months after the last treatment dose.
16. Men must agree to refrain from sperm donation during the study and for 12 months after the last treatment dose
17. Serious medical or psychiatric illness likely to affect participation or that may compromise the ability to give informed consent
18. History of other malignancy that could affect compliance with the protocol or interpretation of results:
18.1. Participants with a history of curatively treated basal or squamous cell carcinoma of the skin, or in situ carcinoma of the cervix at any time prior to the study are eligible
18.2. Participants with low-grade, early-stage prostate cancer (Gleason score 6 or below, Stage 1 or 2) with no requirement for therapy at any time prior to the study are eligible
18.3. Participants receiving adjuvant endocrine therapy for non-metastatic, hormone receptor-positive breast cancer for 2 or more years prior to enrolment are eligible
18.4. Participants with any other malignancy treated with curative intent and in remission without treatment for 2 years prior to enrolment are eligible
19. Any immunotherapy within 4 weeks of the 1st dose of the study
20. Concurrent participation in another therapeutic clinical trial
21. History of clinically significant pneumonitis

Date of first enrolment
01/09/2026

Date of final enrolment
31/03/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Nottingham City Hospital
Hucknall Road
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NG5 1PB

Sponsor information

Organisation
University of Southampton

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type

Funder Name
Genmab

Alternative Name(s)
Genmab A/S

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Denmark

Funder Name
AbbVie

Alternative Name(s)
AbbVie Inc., AbbVie U.S., AbbVie US, Allergan

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date