

# Front-line therapy in CLL: assessment of ibrutinib-containing regimes

<b>Submission date</b> 08/08/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 08/08/2014	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 28/10/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/trials/a-trial-ibrutinib-rituximab-chronic-lymphocytic-leukaemia-flair>

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

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### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2013-001944-76

### Protocol serial number

16675

## Study information

**Scientific Title**

FLAIR: Front-Line therapy in CLL: Assessment of Ibrutinib-containing Regimes: a randomised controlled trial

**Acronym**

FLAIR

**Study objectives**

Current hypothesis as of 13/11/2023

The trial originally aimed to compare the effect on progression-free survival (PFS) of ibrutinib plus rituximab (IR) with that of fludarabine, cyclophosphamide and rituximab (FCR) in patients with previously untreated chronic lymphocytic leukaemia (CLL).

The amendment to include the additional trial arms will allow a comparison of PFS between ibrutinib plus venetoclax (I+V) and ibrutinib alone (I) with FCR, and a comparison of minimal residual disease (MRD) negativity rates in I+V with those in I.

A further amendment to allow genetically high-risk patients, defined by a detectable TP53 disruption (any 17p deletion and/or TP53 mutation), randomised to either I or I+V, will allow a comparison of MRD negativity rates between I and I+V in patients with TP53 abnormalities.

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Previous hypothesis as of 07/09/2018:

The trial originally aimed to compare the effect on progression-free survival (PFS) of ibrutinib plus rituximab (IR) with that of fludarabine, cyclophosphamide and rituximab (FCR) in patients with previously untreated chronic lymphocytic leukaemia (CLL).

The amendment to include the additional trial arms will allow a comparison of PFS between ibrutinib plus venetoclax (I+V) and ibrutinib alone (I) with FCR, and a comparison of minimal residual disease (MRD) negativity rates in I+V with those in I.

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Previous hypothesis:

The trial aims to provide evidence for the future first-line treatment of CLL patients by assessing whether IR is superior to FCR in terms of progression-free survival.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

NRES Committee Yorkshire & The Humber - Leeds West, 17/06/2014, ref: 14/YH/0085

**Study design**

Randomized; Interventional; Design type: Treatment

**Primary study design**

Interventional

**Study type(s)**

Treatment

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

Chronic lymphocytic leukaemia

## Interventions

Current intervention as of 13/11/2023:

All arms are now closed to recruitment.

Participants were randomised on a 1:1:1:1 basis to receive standard therapy with fludarabine, cyclophosphamide and rituximab (FCR), ibrutinib plus rituximab (IR), ibrutinib monotherapy (I) or ibrutinib + venetoclax (I+V).

FCR: fludarabine (oral), cyclophosphamide (oral) and rituximab (intravenous infusion). F (24 mg/m<sup>2</sup>/day) and C (150 mg/m<sup>2</sup>/day) are administered days 1-5 and R is administered at 375 mg/m<sup>2</sup> for day 1 cycle 1 and then at 500 mg/m<sup>2</sup> for day 1 for cycles 2-6. Each cycle is repeated every 28 days and there are 6 cycles.

IR: ibrutinib (oral) and rituximab. 6 cycles of R as per FCR. Ibrutinib (420 mg) is administered daily for 6 years.

I: ibrutinib monotherapy is administered as per IR

I+V: ibrutinib + venetoclax (oral): ibrutinib is administered as per IR. Venetoclax is given daily from week 9 onwards in weekly dose increments (20 mg, 50 mg, 100 mg, 200 mg and 400 mg) after which 400 mg is administered for 6 years.

Follow up: baseline, 9 months post randomisation then every 6 months until 7 years or disease progression. All participants will be followed up at least annually until death.

Participants with any 17p deletion and/or TP53 mutation will be randomised on a 1:1 basis to receive ibrutinib monotherapy (I) or ibrutinib + venetoclax (I+V).

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Previous intervention as of 07/09/2018:

Participants will be randomised on a 1:1:1 basis to receive standard therapy with fludarabine, cyclophosphamide and rituximab (FCR), ibrutinib monotherapy (I) or ibrutinib + venetoclax (I+V).

The IR arm has been closed to recruitment.

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Previous intervention as of 29/06/2017:

Participants will be randomised on a 1:1:1:1 basis to receive standard therapy with fludarabine, cyclophosphamide and rituximab (FCR), ibrutinib plus rituximab (IR), ibrutinib monotherapy (I) or ibrutinib + venetoclax (I+V).

Added 24/07/2017:

FCR: fludarabine (oral), cyclophosphamide (oral) and rituximab (intravenous infusion). F (24mg/m<sup>2</sup>/day) and C (150mg/m<sup>2</sup>/day) are administered days 1-5 and R is administered at 375mg/m<sup>2</sup> for day 1 cycle 1 and then at 500mg/m<sup>2</sup> for day 1 for cycles 2-6. Each cycle is repeated every 28 days and there are 6 cycles.

IR: ibrutinib (oral) and rituximab. 6 cycles of R as per FCR. Ibrutinib (420mg) is administered daily for six years.

I: ibrutinib monotherapy is administered as per IR

I+V: ibrutinib + venetoclax (oral): ibrutinib is administered as per IR. Venetoclax is given daily

from week 9 onwards in weekly dose increments (20mg, 50mg, 100mg, 200mg and 400mg) after which 400mg is administered for six years.

Follow up: baseline, 9 months post randomisation then every six months until 7 years or disease progression. All participants will be followed up at least annually until death.

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Previous intervention:

Participants will be randomised on a 1:1 basis to receive standard therapy with fludarabine, cyclophosphamide and rituximab (FCR) or ibrutinib plus rituximab (IR).

## **Intervention Type**

Drug

## **Phase**

Not Applicable

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

Fludarabine, cyclophosphamide, rituximab, ibrutinib, venetoclax

## **Primary outcome(s)**

Current primary outcome measure as of 07/09/2018:

1. Whether I+V is superior to FCR in terms of progression-free survival.
2. Whether I+V is superior to I in terms of Minimal Residual Disease negativity. The proportion of concurrently randomised participants who are MRD negative in the bone marrow at any time during the trial will be summarised by treatment arm and compared using a binary logistic regression model adjusted for the minimisation factors and trial stage, excluding centre, and Kaplan-Meier curves will be presented. The analysis of MRD negativity will be initially carried out at 2 years after the close of recruitment.

Previous primary outcome measure:

The trial aims to provide evidence for the future first-line treatment of CLL patients by assessing whether IR is superior to FCR in terms of progression-free survival, and whether IR toxicity rates are favourable.

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

Current secondary outcome measures as of 10/09/2018:

1. PFS of I+V in comparison with I. This is assessed using time from randomisation to first documented evidence of disease progression (as defined by IWCLL criteria) or death from any cause. Participants who do not progress will be censored at the last date they were known to be alive and progression-free.
2. PFS of I in comparison with FCR. This is assessed using time from randomisation to first documented evidence of disease progression (as defined by IWCLL criteria) or death from any cause. Participants who do not progress will be censored at the last date they were known to be alive and progression free.
3. Overall survival. This is assessed using time from randomisation to date of death from any cause. Participants not known to have died will be censored at the date they were last known to be alive.
4. Proportion of participants obtaining undetectable MRD, as defined by IWCLL criteria. A negative MRD is defined as the presence of <0.01% CLL cells in the bone marrow. Achievement of MRD negativity is defined as a MRD negative results at any time over the length of the trial.

5. Stopping I-containing therapy in MRD negative patients. Participants receiving I, IR or I+V who achieve MRD negativity in the bone marrow will be able to stop treatment. MRD levels will be monitored over time following stopping treatment.
6. Restarting I-containing therapy on MRD relapse. Those who relapse at the MRD level will restart treatment and will be assessed further for MRD response.
7. Response to therapy, as defined by IWCLL criteria. For participants randomised to FCR or IR, response is assessed at 3 months post-treatment with FCR or R and again at the end of treatment with ibrutinib for participants randomised to IR. For participants randomised to I or I+V, response is assessed at 9 months post-randomisation and again at the end of treatment.
8. Safety and toxicity assessed using adverse events reported throughout the trial, as graded by CTCAE V4.03, and determined by routine clinical assessments at each centre.
9. Health-related quality of life. The EORTC QLQ-C30 and EORTC QLQ-CLL16 will be used to measure participant assessed QoL prior to randomisation, at the end of treatment with FCR and R (for participants randomised to FCR or IR) or at 6 months post-randomisation (for participants randomised to I or I+V), and then at 6-monthly visits.
10. Cost-effectiveness. The SF12 and EQ5D will be used to produce quality adjusted life years (QALYs). NHS resource use and participants' out of pocket expenses will be collected via the Case Record Forms, as well as health economics patient questionnaires. These will be collected prior to randomisation, at the end of treatment with FCR and R (for participants randomised to FCR or IR) or at 6 months post-randomisation (for participants randomised to I or I+V), and then at 6-monthly visits.

Previous secondary outcome measures as of 07/09/2018:

1. PFS of I+V in comparison with I
2. PFS of I in comparison with FCR
3. Overall survival
4. Proportion of participants obtaining undetectable MRD, as defined by IWCLL criteria
5. Stopping of I-containing therapy in MRD-negative patients. Participants who have an MRD negative result in the peripheral blood at any timepoint between 12 and 30 months post-randomisation will be eligible to stop treatment prior to the 6 years post-randomisation timepoint if they confirm MRD negativity in the bone marrow.
6. Time to MRD relapse for participants who stop I-containing treatment based on MRD negativity and then go on to relapse at the MRD
7. Response to therapy, as defined by IWCLL criteria. For each comparison, the best response for each participant at either 3 months post-treatment with FCR, 9 months post randomisation (for participants randomised to I or I+V) or the end of treatment (for I or I+V) will be summarised by treatment group and overall. The proportion of participants achieving a Complete Response (CR+CRi) and an Overall Response (at least a PR) at any stage during the trial will be summarised by treatment arm
8. Safety and toxicity. Safety analyses will summarise the AR, SAE, SAR and SUSAR rates per participant, by treatment received and overall for all participants randomised to stages II and III. ARs will be presented by CTCAE toxicity grade (V4.0.3).
9. Health-related quality of life assessed using all domains of the EORTC QLQ-C30 and the CLL-specific module, EORTC QLQ-CLL16.
10. Cost-effectiveness

Previous secondary outcome measures:

1. Overall survival
2. Undetectable minimal residual disease
3. Response to therapy
4. Health-related quality of life
5. Cost-effectiveness

## Completion date

01/01/2030

# Eligibility

## Key inclusion criteria

Current inclusion criteria as of 13/11/2023:

For standard-risk pathway:

1. At least 18 years old. Maximum age of 75 years old.
2. B-CLL with a characteristic immunophenotype, including small lymphocytic lymphoma
3. Binet's Stages C, B or Progressive Stage A
4. Requiring therapy by the IWCLL criteria in that they must have at least one of the following:
  - 4.1. Evidence of progressive marrow failure as manifested by the development of, or worsening of, anaemia and/or thrombocytopenia.
  - 4.2. Massive (i.e. 6 cm below the left costal margin) or progressive or symptomatic splenomegaly
  - 4.3. Massive nodes (i.e. 10 cm in longest diameter) or progressive or symptomatic lymphadenopathy
  - 4.4. Progressive lymphocytosis with an increase of more than 50% over a 2-month period or lymphocyte doubling time (LDT) of less than 6 months as long as the lymphocyte count is over  $30 \times 10^9/L$
  - 4.5. A minimum of any one of the following disease-related symptoms must be present:
    - 4.5.1. Unintentional weight loss more than or equal to 10% within the previous 6 months.
    - 4.5.2. Significant fatigue (i.e. Eastern Cooperative Oncology Group PS 2 or worse; cannot work or unable to perform usual activities)
    - 4.5.3. Fevers of greater than  $38.0^{\circ}C$  for 2 or more weeks without other evidence of infection
    - 4.5.4. Night sweats for more than 1 month without evidence of infection
5. Considered fit for treatment with FCR as determined by the treating clinician
6. World Health Organisation (WHO) performance status (PS) of 0, 1 or 2
7. Able to provide written informed consent
8. Biochemical values must be within the following limits within 14 days prior to randomization and at baseline:
  - 8.1. Alanine aminotransferase (ALT)  $3 \times$  upper limit of normal (ULN). Aspartate aminotransferase (AST)  $3 \times$  ULN.
  - 8.2. Total bilirubin =  $1.5 \times$  ULN, unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin

For the genetically high-risk pathway

1. TP53 abnormality confirmed by central laboratory
2. At least 18 years old (no upper limit)
3. Meeting all the inclusion criteria for the standard risk pathway stated, with the exception of 'considered fit for treatment with FCR as determined by the treating clinician'

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Previous inclusion criteria:

1. At least 18 years old. Maximum age of 75 years old.
2. B-CLL with a characteristic immunophenotype, including small lymphocytic lymphoma
3. Binets Stages C, B or Progressive Stage A
4. Requiring therapy by the IWCLL criteria in that they must have at least one of the following:
  - 4.1. Evidence of progressive marrow failure as manifested by the development of, or worsening

of, anaemia and/or thrombocytopenia.

4.2. Massive (i.e. 6 cm below the left costal margin) or progressive or symptomatic splenomegaly

4.3. Massive nodes (i.e. 10 cm in longest diameter) or progressive or symptomatic lymphadenopathy

4.4. Progressive lymphocytosis with an increase of more than 50% over a 2-month period or lymphocyte doubling time (LDT) of less than 6 months as long as the lymphocyte count is over  $30 \times 10^9/L$

4.5. A minimum of any one of the following disease-related symptoms must be present:

4.5.1. Unintentional weight loss more than or equal to 10% within the previous 6 months.

4.5.2. Significant fatigue (i.e. Eastern Cooperative Oncology Group PS 2 or worse; cannot work or unable to perform usual activities)

4.5.3. Fevers of greater than  $38.0^{\circ}C$  for 2 or more weeks without other evidence of infection

4.5.4. Night sweats for more than 1 month without evidence of infection

5. Considered fit for treatment with FCR as determined by the treating clinician

6. World Health Organisation (WHO) performance status (PS) of 0, 1 or 2

7. Able to provide written informed consent

8. Biochemical values must be within the following limits within 14 days prior to randomization and at baseline:

8.1. Alanine aminotransferase (ALT) 3 x upper limit of normal (ULN). Aspartate aminotransferase (AST) 3 x ULN.

8.2. Total bilirubin = 1.5 x ULN, unless bilirubin rise is due to Gilberts syndrome or of non-hepatic origin

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

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Key exclusion criteria**

Current exclusion criteria as of 07/09/2018:

1. Prior therapy for CLL

2. History or current evidence of Richter's transformation

3. Major surgery within 4 weeks prior to randomisation

4. Active infection

5. Above 20% P53 deletion, determined by FISH

6. Past history of anaphylaxis following exposure to rat or mouse derived CDR-grafted humanised monoclonal antibodies

7. Concomitant warfarin or equivalent vitamin K inhibitor - added 29/06/2017: or other oral anticoagulant treatment; anyone requiring anticoagulation treatment for greater than 6 months is not eligible for trial entry

8. Pregnancy, lactation or women of child-bearing potential unwilling to use medically approved

contraception whilst receiving treatment and for 12 months after treatment with rituximab has finished, or 30 days after treatment with ibrutinib has finished, whichever is latest. Women must agree to not donate eggs (ova, oocytes) for the purposes of assisted reproduction

9. Men whose partners are capable of having children but who are not willing to use appropriate medically approved contraception whilst receiving treatment and for 12 months after treatment with rituximab has finished, or 3 months after treatment with ibrutinib has finished, whichever is latest, unless they are surgically sterile

10. CNS involvement with CLL

11. Symptomatic cardiac failure not controlled by therapy, or unstable angina not adequately controlled by current therapy (in patients with a significant cardiac history the left ventricular function should be assessed and patients with severe impairment should be excluded)

12. Respiratory impairment (bronchiectasis or moderate COPD)

13. Other severe, concurrent diseases or mental disorders that could interfere with their ability to participate in the study

14. Inability to swallow oral medication

15. Disease significantly affecting gastrointestinal function and/or inhibiting small intestine absorption (malabsorption syndrome, resection of the small bowel, poorly controlled inflammatory bowel disease etc)

16. Known HIV positive

17. Positive serology for Hepatitis B (HB) defined as a positive test for HBsAg. In addition, if negative for HBsAg but HBcAb positive (regardless of HBsAb status), a HB DNA test will be performed and if positive the subject will be excluded

18. Positive serology for Hepatitis C (HC) defined as a positive test for HCAb, in which case reflexively perform a HC RIBA immunoblot assay on the same sample to confirm the result

19. History of prior malignancy, with the exception of the following:

19.1. Malignancy treated with curative intent and with no evidence of active disease present for more than 3 years prior to screening and felt to be at low risk for recurrence by treating physician

19.2. Adequately treated non-melanomatous skin cancer or lentigo maligna melanoma without current evidence of disease

19.3. Adequately treated cervical carcinoma in situ without current evidence of disease

20. Persisting severe pancytopenia (neutrophils  $<0.5 \times 10^9/l$  or platelets  $<50 \times 10^9/l$ ) unless due to direct marrow infiltration by CLL

21. Current treatment with prednisolone of  $>10$  mg/day

22. Active haemolysis (patients with haemolysis controlled with prednisolone at a dose 10 mg or less per day can be entered into the trial)

23. Patients with a creatinine clearance of less than 30 ml/min (either measured or derived by the Cockcroft Gault formula or alternative locally approved formula)

24. History of stroke or intracranial hemorrhage within 6 months prior to enrollment

25. Requirement for treatment with a strong CYP3A4/5 inhibitor or inducer

26. Cardiac event (eg. recent myocardial infarction, coronary artery stent) requiring dual antiplatelet treatment.

27. Allergy or inability to tolerate uric acid reducing agents (eg allopurinol/rasburicase).

28. Unwilling or unable to take PCP prophylaxis (eg cotrimoxazole).

Previous exclusion criteria:

1. Prior therapy for CLL

2. History or current evidence of Richters transformation

3. Major surgery within 4 weeks prior to randomisation

4. Active infection

5. Above 20% P53 deletion, determined by FISH

6. Past history of anaphylaxis following exposure to rat or mouse derived CDR-grafted



humanised monoclonal antibodies

7. Concomitant warfarin or equivalent vitamin K inhibitor - added 29/06/2017: or other oral anticoagulant treatment; anyone requiring anticoagulation treatment for greater than 6 months is not eligible for trial entry

8. Pregnancy, lactation or women of child-bearing potential unwilling to use medically approved contraception whilst receiving treatment and for 12 months after treatment with rituximab has finished, or 30 days after treatment with ibrutinib has finished, whichever is latest. Women must agree to not donate eggs (ova, oocytes) for the purposes of assisted reproduction

9. Men whose partners are capable of having children but who are not willing to use appropriate medically approved contraception whilst receiving treatment and for 12 months after treatment with rituximab has finished, or 3 months after treatment with ibrutinib has finished, whichever is latest, unless they are surgically sterile

10. CNS involvement with CLL

11. Symptomatic cardiac failure not controlled by therapy, or unstable angina not adequately controlled by current therapy (in patients with a significant cardiac history the left ventricular function should be assessed and patients with severe impairment should be excluded)

12. Respiratory impairment (bronchiectasis or moderate COPD)

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19. History of prior malignancy, with the exception of the following:

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19.2. Adequately treated non-melanomatous skin cancer or lentigo maligna melanoma without current evidence of disease

19.3. Adequately treated cervical carcinoma in situ without current evidence of disease

20. Persisting severe pancytopenia (neutrophils  $<0.5 \times 10^9/l$  or platelets  $<50 \times 10^9/l$ ) unless due to direct marrow infiltration by CLL

21. Current treatment with prednisolone of  $>10$  mg/day

22. Active haemolysis (patients with haemolysis controlled with prednisolone at a dose 10 mg or less per day can be entered into the trial)

23. Patients with a creatinine clearance of less than 30 ml/min (either measured or derived by the Cockcroft Gault formula or alternative locally approved formula)

24. History of stroke or intracranial hemorrhage within 6 months prior to enrollment

25. Requirement for treatment with a strong CYP3A4/5 inhibitor or inducer

**Date of first enrolment**

01/09/2014

**Date of final enrolment**

31/10/2023

# Locations

## **Countries of recruitment**

United Kingdom

England

Northern Ireland

Scotland

Wales

## **Study participating centre**

### **Clinical Trials Research Unit (CTRU)**

Leeds

United Kingdom

LS2 9JT

## **Study participating centre**

### **Aberdeen Royal Infirmary**

Foresterhill Road

Aberdeen

United Kingdom

AB25 2ZN

## **Study participating centre**

### **Addenbrookes Hospital**

Hills Road

Cambridge

United Kingdom

CB2 0QQ

## **Study participating centre**

### **Altnagelvin Hospital**

WHST

Glenshane Road

Glenshane

Londonderry

United Kingdom

BT47 6SB

**Study participating centre**

**Barnet General Hospital**

Wellhouse Lane  
Hertfordshire  
Barnet  
United Kingdom  
EN5 3DJ

**Study participating centre**

**Colchester General Hospital**

Department of Haematology  
Colchester General Hospital  
Turner Road  
Colchester  
Essex  
Colchester  
United Kingdom  
CO4 5JL

**Study participating centre**

**Basingstoke and North Hampshire Hospital**

Aldermaston Road  
Basingstoke  
United Kingdom  
RG24 9NA

**Study participating centre**

**Royal Hampshire County Hospital**

Romsey Road  
Winchester  
United Kingdom  
SO22 5DG

**Study participating centre**

**Beatson Oncology Centre**

1053 Great Western Road  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**  
**Victoria Hospital, Glasgow**  
52 Grange Road  
Glasgow  
United Kingdom  
G42 9LF

**Study participating centre**  
**Royal Alexandra Hospital**  
Corsebar Road  
Paisley  
United Kingdom  
PA2 9PN

**Study participating centre**  
**Belfast City Hospital**  
Belfast Health and Social Care Trust  
51 Lisburn Road  
Belfast  
United Kingdom  
BT9 7AB

**Study participating centre**  
**Birmingham Heartlands Hospital**  
Birmingham  
United Kingdom  
B9 5SS

**Study participating centre**  
**Good Hope Hospital**  
Rectory Road  
Sutton Coldfield  
United Kingdom  
B75 7RR

**Study participating centre**  
**Blackpool Victoria Hospital**  
Whinney Heys Road  
Lancashire

Blackpool  
United Kingdom  
FY3 8NR

**Study participating centre**  
**Borders General Hospital**  
Melrose  
United Kingdom  
TD6 9BS

**Study participating centre**  
**Bradford Royal Infirmary**  
Bradford Teaching Hospitals NHS Foundation Trust  
Duckworth Lane  
West Yorkshire  
BD9 6RJ  
Bradford  
United Kingdom  
BD9 6RJ

**Study participating centre**  
**Bristol Haematology and Oncology Centre**  
Horfield Road  
Bristol  
United Kingdom  
BS2 8ED

**Study participating centre**  
**Calderdale Royal Hospital**  
Salterhebble  
Halifax  
United Kingdom  
HX3 0PW

**Study participating centre**  
**Huddersfield Royal Infirmary**  
Acre Street  
Lindley  
Huddersfield  
United Kingdom  
HD3 3EA

**Study participating centre**

**Castle Hill Hospital**

Castle Road  
Cottingham  
United Kingdom  
HU16 5JQ

**Study participating centre**

**Gloucestershire Royal Hospital**

Great Western Road  
Gloucester  
United Kingdom  
GL1 3NN

**Study participating centre**

**Cheltenham General Hospital**

Sandford Road  
Cheltenham  
United Kingdom  
GL53 7AN

**Study participating centre**

**Christie Hospital**

Christie NHS Foundation Trust  
Wilmslow Road  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**

**Churchill Hospital**

Oxford Cancer Centre & Cancer Research UK  
Oxford University Hospitals NHS Trust  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**

**Basildon Hospital**

Basildon  
United Kingdom  
SS16 5NL

**Study participating centre****Countess of Chester Hospital**

Chester  
United Kingdom  
CH2 1UL

**Study participating centre****Craigavon Area Hospital**

68 Lurgan Road  
Portadown  
United Kingdom  
BT63 5QQ

**Study participating centre****Croydon University Hospital**

530 London Road  
Croydon  
United Kingdom  
CR7 7YE

**Study participating centre****Derriford Hospital**

Plymouth  
United Kingdom  
PL6 8DH

**Study participating centre****Doncaster Royal Infirmary**

Armthorpe Road  
Doncaster  
United Kingdom  
DN2 5LT

**Study participating centre**

**East Surrey Hospital**

Canada Avenue  
Redhill  
Surrey  
Redhill  
United Kingdom  
RH1 5RH

**Study participating centre****Epsom General Hospital**

Dorking Road  
Epsom  
United Kingdom  
KT18 7EG

**Study participating centre****St Helier Hospital**

Wrythe Lane  
Carshalton  
United Kingdom  
SM5 1AA

**Study participating centre****George Eliot Hospital**

College Street  
Nuneaton  
United Kingdom  
CV10 7DJ

**Study participating centre****Glan Clwyd Hospital**

Bodelwyddan  
Rhyl  
United Kingdom  
LL18 5UJ

**Study participating centre****Lincoln County Hospital**

Haematology Department  
Lincoln County Hospital  
Greetwell Road



Lincoln  
Lincolnshire (E Mid)  
Lincoln  
United Kingdom  
LN2 5QY

**Study participating centre**  
**Grantham & District Hospital**  
Manthorpe Road  
Grantham  
United Kingdom  
NG31 8DG

**Study participating centre**  
**Pilgrim Hospital**  
Sibsey Road  
Boston  
United Kingdom  
PE21 9QS

**Study participating centre**  
**Harrogate District Hospital**  
Lancaster Park Road  
Harrogate  
United Kingdom  
HG2 7SX

**Study participating centre**  
**Hammersmith Hospital**  
Imperial College Healthcare NHS Trust  
Du Cane Road  
London  
United Kingdom  
W12 0HS

**Study participating centre**  
**Ipswich Hospital**  
Ipswich Hospital NHS Trust  
Heath Road  
Suffolk  
Ipswich

United Kingdom  
IP4 5PD

**Study participating centre**  
**James Cook University Hospital**  
Marton Road  
Middlesbrough  
United Kingdom  
TS4 3BW

**Study participating centre**  
**James Paget Hospital**  
Great Yarmouth  
United Kingdom  
NR31 6LA

**Study participating centre**  
**Kings College Hospital**  
Denmark Hill  
London  
United Kingdom  
SE5 9RS

**Study participating centre**  
**Princess Royal University Hospital**  
Farnborough Common  
Orpington  
United Kingdom  
BR6 8ND

**Study participating centre**  
**Kings Mill Hospital**  
Mansfield Road  
Nottinghamshire  
Sutton-In-Ashfield  
United Kingdom  
NG17 4JL

**Study participating centre**

**Leicester Royal Infirmary**  
Leicester General Infirmary  
Gwendolen Road  
Leicester  
LE5 4PW  
Leicester  
United Kingdom  
LE5 4PW

**Study participating centre**  
**Manchester Royal Infirmary**  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**  
**Milton Keynes General Hospital**  
Standing Way  
Eaglestone  
Milton Keynes  
United Kingdom  
MK6 5LD

**Study participating centre**  
**Monklands Hospital**  
Monkscourt Avenue  
Airdrie  
United Kingdom  
ML6 0JS

**Study participating centre**  
**Musgrove Park Hospital**  
Taunton  
United Kingdom  
TA1 5DA

**Study participating centre**  
**Nevill Hall Hospital**  
Brecon Road  
Abergavenny

United Kingdom  
NP7 7EG

**Study participating centre**  
**Northampton General Hospital**  
Northampton  
United Kingdom  
NN1 5BD

**Study participating centre**  
**Nottingham University Hospitals**  
City Hospital Campus  
Hucknall Road  
Nottingham  
United Kingdom  
NG5 1PB

**Study participating centre**  
**Peterborough City Hospital**  
Peterborough & Stamford NHS FT  
Bretton Gate  
Peterborough  
United Kingdom  
PE3 9GZ

**Study participating centre**  
**Poole Hospital**  
Poole Hospital NHS Foundation Trust  
Longfleet Road  
Dorset  
Poole  
United Kingdom  
BH15 2JB

**Study participating centre**  
**Royal Bournemouth Hospital**  
Castle Lane East  
Bournemouth  
United Kingdom  
BH7 7DW

**Study participating centre**

**Queen Elizabeth Hospital Birmingham**

University Hospital Birmingham NHS Foundation Trust  
Queen Elizabeth Hospital  
Queen Elizabeth Medical Centre  
Edgbaston  
Birmingham  
United Kingdom  
B15 2TH

**Study participating centre**

**Queen Elizabeth Hospital Gateshead**

Sheriff Hill  
Gateshead  
United Kingdom  
NE9 6SX

**Study participating centre**

**Queen's Hospital Romford**

Haematology & Oncology Department  
Queens Hospital  
Rom Valley Way  
Essex  
Romford  
United Kingdom  
RM7 0AG

**Study participating centre**

**Raigmore Hospital**

Department of Haematology  
Old Perth Road  
Inverness  
United Kingdom  
IV2 3UJ

**Study participating centre**

**Rotherham District General Hospital**

Moorgate Road  
Oakwood  
Rotherham  
S60 2UD

Rotherham  
United Kingdom  
S60 2UD

**Study participating centre**  
**Queen Alexandra Hospital**  
Portsmouth  
United Kingdom  
PO6 3LY

**Study participating centre**  
**Royal Cornwall Hospital**  
Truro  
United Kingdom  
TR1 3LJ

**Study participating centre**  
**Royal Derby Hospital**  
Uttoxeter Road  
Derby  
United Kingdom  
DE22 3NE

**Study participating centre**  
**Royal Devon and Exeter Hospital**  
Barrack Road  
Devon  
Exeter  
United Kingdom  
EX2 5DW

**Study participating centre**  
**Royal Gwent Hospital**  
Block 3, Pathology  
Royal Gwent Hospital  
Newport  
Gwent  
NP20 2UB  
Newport  
United Kingdom  
NP20 2UB

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

**Study participating centre**  
**Royal Lancaster Infirmary**  
Ashton Road  
Lancaster  
United Kingdom  
LA1 4RP

**Study participating centre**  
**Royal Liverpool University Hospital**  
Prescot Street  
Liverpool  
United Kingdom  
L7 8XP

**Study participating centre**  
**Royal Marsden Hospital**  
London  
London  
United Kingdom  
SW3 6JJ

**Study participating centre**  
**Royal Oldham Hospital**  
Central Admin, Pennine Square  
Rochdale Road  
Oldham  
United Kingdom  
OL1 2JH

**Study participating centre**

**Royal Stoke University Hospital**  
Stoke-on-Trent  
United Kingdom  
ST4 6QG

**Study participating centre**  
**Royal Surrey County Hospital**  
Egerton Road  
Guildford  
United Kingdom  
GU2 7XX

**Study participating centre**  
**Royal United Hospital**  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**  
**Russells Hall Hospital**  
Georgina Unit  
High Street  
Pensnett  
Dudley  
United Kingdom  
DY1 2HQ

**Study participating centre**  
**Salford Royal Hospital**  
Salford Royal Hospital NHS Foundation Trust  
Stott Lane  
Salford  
Manchester  
M6 8HD  
Salford  
United Kingdom  
M6 8HD

**Study participating centre**  
**Salisbury District Hospital**  
Salisbury



United Kingdom  
SB2 8BJ

**Study participating centre**  
**Sandwell General Hospital**  
Lyndon  
West Midlands  
West Bromwich  
United Kingdom  
B71 4HJ

**Study participating centre**  
**Scunthorpe General Hospital**  
Cliff Gardens  
Scunthorpe  
United Kingdom  
DN15 7BH

**Study participating centre**  
**Diana, Princess of Wales Hospital**  
Scartho Road  
Grimsby  
United Kingdom  
DN33 2BA

**Study participating centre**  
**Singleton Hospital**  
Sketty Lane  
Swansea  
United Kingdom  
SA2 8QA

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

**Study participating centre**  
**St Bartholomew's Hospital**  
West Smithfield  
London  
United Kingdom  
EC1A 7BE

**Study participating centre**  
**St. James's University Hospital**  
Department of Haematology, Level 3 Bexley Wing  
St. James's University Hospital  
Beckett Street  
Leeds  
United Kingdom  
LS9 7TF

**Study participating centre**  
**St George's Hospital**  
London  
United Kingdom  
SW17 0QT

**Study participating centre**  
**Stoke Mandeville Hospital**  
CCHU  
Mandeville Road  
Buckinghamshire  
Aylesbury  
United Kingdom  
HP21 8AL

**Study participating centre**  
**Torbay District General Hospital**  
Lawes Bridge  
South Devon  
Torquay  
United Kingdom  
TQ2 7AA

**Study participating centre**

**University College London Hospital**  
235 Euston Road  
London  
United Kingdom  
NW1 2BU

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

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

**Study participating centre**  
**University Hospital Coventry**  
Clifford Bridge Road  
Coventry  
United Kingdom  
CV2 2DX

**Study participating centre**  
**Victoria Hospital Kirkcaldy**  
Fife Area Labs  
Victoria Hospital (Kirkcaldy)  
Hayfield Road  
Kirkcaldy  
Fife  
KY2 5AH  
Kirkcaldy  
United Kingdom  
KY2 5AH

**Study participating centre**

**Queen Margaret Hospital**

Whitefield Road  
Dunfermline  
United Kingdom  
KY12 0SU

**Study participating centre**

**Watford General Hospital**

Watford  
United Kingdom  
WD18 0HB

**Study participating centre**

**West Middlesex University Hospital**

Isleworth  
United Kingdom  
TW7 6AF

**Study participating centre**

**West Wales General Hospital**

Glangwili General Hospital, Chemotherapy Day Unit, Dolgwili Road, Carmarthen, SA31 2AF  
Glangwili General Hospital  
Dolgwilli Road  
Carmarthen  
Carmarthenshire  
SA31 2AF  
Carmarthen  
United Kingdom  
SA31 2AF

**Study participating centre**

**Western General Hospital**

Crewe Road  
Edinburgh  
United Kingdom  
EH4 2XU

**Study participating centre**

**Worcestershire Royal Hospital**

Charles Hastings Way  
Worcester

United Kingdom  
WR5 1DD

**Study participating centre**

**Worthing Hospital**

Lyndhurst Road  
Worthing  
United Kingdom  
BN11 2DH

**Study participating centre**

**St Richards Hospital**

Spitalfield Lane  
Chichester  
United Kingdom  
PO19 6SE

**Study participating centre**

**Wythenshawe Hospital**

Department of Haematology  
University Hospital of South Manchester NHS Foundation Trust  
Southmoor Road  
Wythenshawe  
Manchester  
United Kingdom  
M23 9LT

**Study participating centre**

**York Hospital**

Wigginton Road  
York  
United Kingdom  
YO31 8HE

**Study participating centre**

**Ysbyty Gwynedd**

Penrhosgarnedd  
Bangor  
United Kingdom  
LL57 1PW

**Study participating centre**  
**Ysbyty Maelor**  
Wrexham Maelor Hospital  
Croesnewydd Road  
Wrexham  
United Kingdom  
LL13 7TD

## Sponsor information

**Organisation**  
University of Leeds (UK)

**ROR**  
<https://ror.org/024mrx33>

## Funder(s)

**Funder type**  
Charity

**Funder Name**  
Cancer Research UK; Grant Codes: C18027/A15790

**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

**Funder Name**  
Janssen Pharmaceuticals

**Alternative Name(s)**

Janssen Pharmaceutica NV, JANSSEN-CILAG NV, Janssen Belgium, Janssen, Janssen Pharmaceuticals

### Funding Body Type

Private sector organisation

### Funding Body Subtype

For-profit companies (industry)

### Location

Belgium

### Funder Name

AbbVie Ltd

## Results and Publications

### Individual participant data (IPD) sharing plan

Individual participant data for all trial participants (excluding any trial-specific participant opt-outs) will be made available for secondary research purposes at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will only be shared for participants who have given consent to use of their data for secondary research.

Requests to access trial data should be made to CTRU-DataAccess@leeds.ac.uk in the first instance. Requests will be reviewed (based on the above principles) by relevant stakeholders. No data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention requirements, which will usually stipulate that data recipients must delete their copy of the data at the end of the planned project.

### IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	protocol	10/12/2023	19/12/2023	Yes	No
<a href="#">Results article</a>		15/06/2025	17/06/2025	Yes	No
<a href="#">Protocol article</a>		22/08/2017		Yes	No
<a href="#">Protocol article</a>	protocol update	08/01/2021	11/01/2021	Yes	No
<a href="#">HRA research summary</a>	interim results		28/06/2023	No	No
<a href="#">Interim results article</a>		04/05/2023	09/05/2023	Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Plain English results</a>			28/10/2025	No	Yes