ISRCTN61925716 https://doi.org/10.1186/ISRCTN61925716

# Best available therapy versus JAK Inhibition in patients with high risk polycythaemia vera or essential thrombocythaemia who are resistant or intolerant to hydroxycarbamide

| | | |
|---|---|---|
| **Submission date**<br>12/04/2012 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[_] Protocol |
| **Registration date**<br>12/04/2012 | **Overall study status**<br>Completed | [_] Statistical analysis plan<br>[X] Results |
| **Last Edited**<br>30/06/2023 | **Condition category**<br>Cancer | [_] Individual participant data |

**Plain English summary of protocol**
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-ruxolitinib-treat-polycytheaemia-vera-essential-thrombocythaemia-majic

## Contact information

**Type(s)**
Scientific

**Contact name**
Mrs Sonia Fox

**Contact details**
Edgbaston
Birmingham
United Kingdom
B15 2TT
-
MAJIC@trials.bham.ac.uk

## Additional identifiers

**Clinical Trials Information System (CTIS)**
2011-005279-18

**Protocol serial number**
11941

# Study information

## Scientific Title
A randoMised study of best Available therapy versus JAK Inhibition in patients with high risk polycythaemia vera or essential thrombocythaemia who are resistant or intolerant to hydroxyCarbamide

## Acronym
MAJIC

## Study objectives
MAJIC is a phase II, randomised, open-label, two arm, multicentre clinical trial. The trial aims to investigate and evaluate the activity and safety (in terms of complete haematological response within one year) of Ruxolitinib in the treatment of patients with Polycythaemia Vera (PV) or Essential Thrombocythaemia (ET) who have met criteria for resistance or intolerance of hydroxycarbamide (HC) therapy.

More information can be found at http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=11941

On 10/03/2015 the overall trial end date was changed from 02/12/2013 to 31/07/2020.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
NRES Committee North West - Liverpool Central, 25/01/2012, ref: 12/NW/0045

## Primary study design
Interventional

## Study design
Randomised; Interventional; Design type: Treatment

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Haematological Oncology; Disease: Miscellaneous

## Interventions
1. Ruxolitinib, JAK I/II inhibitor
2. Best Available Therapy: This would be the clinicians choice of second line treatment that the patient would receive outside of the trial. This can be any active (non investigational) agent used alone or in combination but not solely venesection or supportive care.

Follow Up Length: 60 month(s)
Study Entry : Single Randomisation only

### Intervention Type
Drug

### Phase
Phase II

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

### Primary outcome(s)
Complete response rates within 1 year

### Key secondary outcome(s)
1. Partial response rates as defined by European LeukemiaNet criteria within 1 year of treatment
2. Duration of response
3. Toxicity profile of Ruxolitinib based on CTC criteria
4. Dose Intensity
5. Histological response: bone marrow biopsy analysis criteria as defined by European LeukemiaNet
6. Molecular response: JAK2V617F status quantitation; criteria defined by European LeukemiaNet
7. Haemorrhagic and thromboembolic event rate
8. Quality of life and disease symptom burden
9. Overall survival
10. Progression free survival

### Completion date
28/03/2022

## Eligibility

### Key inclusion criteria
Inclusion criteria for PV:
1. Male or female patient >=18 years of age
2. A confirmed diagnosis of high risk PV. High Risk is defined as ANY ONE of the following
2.1. Age >60 years
2.2. Previous documented thrombosis
2.3. Erythromelalgia or migraine (severe, recurrent, requiring medications, and felt to be secondary to the MPN) either after diagnosis or within 10 years before diagnosis and considered to be disease-related
2.4. Significant splenomegaly (i.e. > 5cm below costal margin on palpation) or symptomatic (splenic infarcts or requiring analgesia)
2.5. Platelets > 1000 x 10^9/L
2.6. Diabetes or hypertension requiring pharmacological therapy for > 6 months

Inclusion criteria for ET:
1. Male or female patient >=18 years of age
2. A confirmed diagnosis of high risk ET. High risk is defined as ANY ONE of the following:
2.1. Age > 60 years
2.2. Platelet count > 1500 x 10^9/L
2.3. Previous documented thrombosis

2.4. Erythromelalgia or migraine (severe, recurrent, requiring medications, and felt to be secondary to the MPN) either after diagnosis or within 10 years before diagnosis and considered to be disease-related
2.5. Previous haemorrhage related to ET Diabetes or hypertension requiring pharmacological therapy for > 6 months
3. ALL patients must also be either intolerant OR resistant to Hydroxycarbamide (HC) based on the following established criteria: Any ONE of the following:
3.1. Platelet count >600 x 10^9/L after 8 weeks of at least 2 g/day or maximum tolerated dose (MTD) of HC (2.5 g/day in patients with a body weight>80 kg)
3.2. Platelet count >400 x 10^9/L and WBC < 2.5 x 10^9/L at any dose of HC (for a period of at least 8 weeks)
3.3. Platelet count >400 x 10^9/L and Hb < 11 g/dl at any dose of HC (for a period of at least 8 weeks)
3.4. Platelet count persistently <100 x 109/L at any dose of HC (for a period of at least 8 weeks)
3.4. Progressive splenomegaly or hepatomegaly i.e. enlargement by more than 5cm or appearance of new splenomegaly or hepatomegaly on HC treatment
3.5. Not achieving the desired reduction of haematocrit or packed cell volume with the addition of HC in patients who do not tolerate frequent venesections after 8 weeks of at least 2 g/day of HC (2.5 g/day in patients with a body weight >80 kg)
3.6. Not achieving the desired stable reduction of WBC when leukocytes are a target of therapy after 8 weeks of at least 2 g/day or MTD of HC (2.5 g/day in patients with a body weight>80 kg)
3.7. Thrombosis or haemorrhage while on therapy
3.8. Presence of leg ulcers or other unacceptable HC-related non-haematological toxicities, such as unacceptable mucocutaneous manifestations, gastrointestinal symptoms, pneumonitis or fever at any dose of HC OR Cycling platelet counts on therapy
Target Gender: Male & Female ; Lower Age Limit 18 years

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
18 Years

## Sex
All

## Total final enrolment
306

## Key exclusion criteria
1. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry)
2. Patients and partners of childbearing potential not willing to use effective contraception
3. Eastern Cooperative Oncology Group Performance Status Scale (ECOG) Performance Status Score >= 3

4. Current rapid or paroxysmal atrial fibrillation
5. Uncontrolled or unstable angina
6. Recent (6 months) myocardial infarction or acute coronary syndrome or any clinically significant cardiac disease > New York Heart Association (NYHA) Class II
7. Previous treatment with a Janus kinase 2 (JAK2) inhibitor
8. Previous (within the last 12 months) or current platelet count <100 x 10^9/L or neutrophil count < 1 x 10^9/L not due to therapy
9. Inadequate liver function as defined by aspartate aminotransferase/alanine aminotransferase (ALT/AST) >1.5 x upper limit normal (ULN)
10. Inadequate renal function as defined by Glomerular filtration rate (GFR) < 15 mls/min
11. Unable to give informed consent

### Date of first enrolment
04/06/2012

### Date of final enrolment
31/07/2015

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**University of Birmingham**
Birmingham
United Kingdom
B15 2TT

## Sponsor information

### Organisation
University of Birmingham (UK)

### ROR
https://ror.org/03angcq70

## Funder(s)

### Funder type
Charity

**Funder Name**
Leukaemia & Lymphoma Research (UK)

# Results and Publications

## Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Trial Management Group (contact majic@trials.bham.ac.uk) who will review any requests for data sharing following the end of trial report in 2022.

## IPD sharing plan summary
Available on request

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 01/07/2023 | 30/06/2023 | Yes | No |
| Basic results | | 29/03/2023 | 29/03/2023 | No | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Plain English results | | | 25/10/2022 | No | Yes |