

A Phase Ib study of eltrombopag and azacitidine in patients with high risk myelodysplastic syndromes and related disorders

Submission date 05/07/2013	Recruitment status No longer recruiting	☒ Prospectively registered ☐ Protocol
Registration date 05/07/2013	Overall study status Completed	☐ Statistical analysis plan ☒ Results
Last Edited 21/07/2022	Condition category Cancer	☐ Individual participant data

Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/trials/trials-search/a-trial-eltrombopag-azacitidine-myelodysplastic-syndrome-elastic>

Contact information

Type(s)

Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2013-000341-39

Protocol serial number

Study information

Scientific Title

A Phase Ib study of eltrombopag and azacitidine in patients with high risk myelodysplastic syndromes and related disorders

Acronym

ELASTIC

Study objectives

ELASTIC is a 3+3 cohort trial designed to evaluate the Maximum Tolerated Dose (MTD) and Optimal Biological Dose (OBD) of eltrombopag in combination with azacitidine. This trial will recruit patients with IPSS INT-2/high-risk Myelodysplastic Syndromes (MDS), Chronic Myelomonocytic Leukaemia (CMML-2) and Acute Myeloid Leukaemia (AML) with less than 30% blasts.

The objectives of the trial are to evaluate the safety and tolerability of the oral thrombopoietin receptor agonist eltrombopag in combination with azacitidine in patients with advanced MDS and establish the Maximum Tolerated Dose (MTD) and Optimum Biological Dose (OBD). The trial will also aim to investigate the effect of eltrombopag with azacitidine on the fate of MDS/AML stem cell progenitors from patients so treated. The feasibility of Leukaemic Stem Cell (LSC) tracking as a marker of response and predictor of treatment failure in future Phase II/III studies will be explored.

A maximum of 27 patients will be recruited to the 3+3 dose finding component of the study and a minimum of 3. The number of patients recruited is determined by the maximum dose of 300mg.

An additional 10 patients will then be recruited at the MTD to allow a preliminary estimate of activity.

A maximum of 37 patients in total will be recruited to this study.

Ethics approval required

Old ethics approval format

Ethics approval(s)

13/SC/0309; First MREC approval date 28/06/2013

Primary study design

Interventional

Study design

Non-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

Azacitidine, Hypomethylating agent used within its licensed indication; Eltrombopag, Thrombopoietin receptor (TpoR) agonist; Follow Up Length: 7 month(s); Study Entry : Registration only

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

Eltrombopag, azacitidine

Primary outcome(s)

Safety and tolerability of eltrombopag in combination with azacitidine; Timepoint(s): Within 5 weeks (1 cycle) of azacitidine treatment

Key secondary outcome(s)

1. To establish the Optimal Biological dose (OBD) of eltrombopag in combination with azacitidine; Timepoint(s): Within 5 weeks (1 cycle) of azacitidine treatment
2. To evaluate evidence for a dose response effect of eltrombopag on bone marrow blast percentage; Timepoint(s): During 3 cycles of azacitidine treatment
3. To evaluate the activity of eltrombopag plus azacitidine per IWG 2006 response criteria for MDS; Timepoint(s): During 3 cycles of azacitidine treatment
4. To evaluate the dosage effect of eltrombopag on stem/progenitor subset numbers and fate; Timepoint(s): During 3 cycles of azacitidine treatment
5. To evaluate the effect of eltrombopag on azacitidine treatment delays and dose reductions; Timepoint(s): During 3 cycles of azacitidine treatment
6. To evaluate the effect of eltrombopag on bleeding complications; Timepoint(s): During 3 cycles of azacitidine treatment
7. To evaluate the effect of eltrombopag on platelet counts; Timepoint(s): During 3 cycles of azacitidine treatment
8. To evaluate the effect of eltrombopag on the need for platelet transfusions; Timepoint(s): During 3 cycles of azacitidine treatment

Completion date

31/08/2020

Eligibility

Key inclusion criteria

1. Age ≥ 16 years of age
2. Platelet count at baseline $< 150 \times 10^9/l$
3. Myelodysplastic Syndromes (MDS) classified as Intermediate 2 risk or high risk according to the International Prognostic Scoring System (IPSS) at registration or Chronic Myelomonocytic Leukaemia (CMML) with 10-29% bone marrow blasts without proliferation (peripheral white blood cell count $< 13 \times 10^9/l$) or Acute Myeloid Leukaemia (AML) with 20-30% bone marrow blast
4. Subjects must have platelet count and platelet transfusion data available over a period of 4 weeks prior to registration

5. A baseline bone marrow examination to evaluate blast percentage, karyotype and assessment of fibrotic change within 8 weeks of registration
 6. Alanine Aminotransferase ALT/Aspartate Aminotransferase (AST) < 3 x upper limit of normal
ECOG = 2
 7. Valid informed consent
- Target Gender: Male & Female ; Lower Age Limit 16 years

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Total final enrolment

31

Key exclusion criteria

1. AML with >30% blasts
2. Known HIV positive
3. Known liver cirrhosis
4. Uncontrolled infection (grade 4 CTCAE v4)
5. Previous exposure to azacitidine
6. Previous exposure to thrombomimetic agents
7. Use of prior investigational agents within 6 weeks
8. Other severe, concurrent diseases or mental disorders
9. Concurrent active or previous malignancy within the last 3 years except controlled, localised prostate cancer on hormone therapy or non-melanoma skin malignancy or cervical carcinoma in situ or completely resected colonic polyps carcinoma in situ
10. Bone marrow fibrosis
11. Clinical evidence of splenomegaly
12. Known hypersensitivity to study drugs or any of their excipients
13. Pregnant and lactating patients (patients of childbearing potential must have a negative pregnancy test prior to study entry)
14. Females of childbearing potential (i.e. not postmenopausal or surgically sterilised) who are not willing to use adequate methods of contraception to prevent pregnancy or abstain from heterosexual activity for the duration of the trial and for at least 3 months following treatment discontinuation.
15. Male patients who are not willing to use an adequate method of contraception for the duration of the trial treatment if engaged in sexual activity with a female of childbearing potential and for at least 3 months following treatment discontinuation
16. Patients of east Asian ancestry*

* Patients will be excluded if either parent is East Asian (such as Chinese, Japanese, Taiwanese or Korean). In previous studies, the pharmacokinetics of eltrombopag in patients of East Asian ancestry differs significantly from the non-East Asian patients. The SPC for eltrombopag recommends patients receive 50% of the recommended dose. As this is a dose finding study,

inclusion of these patients may impair an accurate finding of MTD and OBD that could be applied to the UK population.

Date of first enrolment

02/09/2013

Date of final enrolment

05/10/2015

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

University of Birmingham

Birmingham

United Kingdom

B15 2TT

Sponsor information

Organisation

University of Birmingham

ROR

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

Funder(s)

Funder type

Charity

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

The Cancer Research UK Clinical Trials Unit (CRCTU) is committed to responsible and controlled sharing of anonymised clinical trial data with the wider research community to maximise potential patient benefit while protecting the privacy and confidentiality of study participants. A summary of the clinical trial results is already available.

Participant data and the associated supporting documentation will typically be available for all CRCTU clinical trials within 6 months after the publication of the outcome measures. Only scientifically sound proposals from appropriately qualified research groups will be considered for data sharing. Data Sharing Requests will be reviewed independently by the CRCTU Directors in discussion with the Chief Investigator and relevant Trial Management Group and due diligence checks will be performed.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	Cancer Research UK summary of results	23/09/2021	20/05/2022	No	No
HRA research summary			28/06/2023	No	No
Plain English results			21/07/2022	No	Yes