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A phase II study of the use of azacitidine for the treatment of patients with chronic graft-versus-host-disease

Submission date
21/11/2016

Recruitment status
No longer recruiting

Registration date
21/11/2016

Overall study status
Completed

Last Edited
18/12/2023

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-using-azacitidine-for-people-with-chronic-graft-versus-host-disease-aztec

Study website
www.birmingham.ac.uk/aztec

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2014-005659-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
19722

Study information

Scientific Title
A phase II study of the use of azacitidine for the treatment of patients with chronic graft--versus--host-disease who have failed therapy with corticosteroids

Acronym
AZTEC

Study objectives
The aim of this study is to determine the value of azacitidine in patients with chronic graft--versus--host-disease (GvHD) who do not respond to, or have become dependent on, steroids.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands- Nottingham 2 Research Ethics Committee, 21/10/2015, ref: 15/EM/044

Study design
Non-randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Chronic graft--versus--host-disease

Interventions
All patients will receive treatment with 36mg/m2 of azacitidine of days 1-5 of each cycle. Each cycle will last 28 days. Azacitidine may be administered via subcutaneous injection or

intravenously. Patients will receive 6 cycles of azacitidine treatment. Patients may continue beyond 6 cycles (maximum of 10) if clinical benefit is observed. The patients will be followed up for 6 months after the last treatment with azacitidine. The maximum duration the patient will be on study is 16 months.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Best overall response (complete or partial) (GvHD) within 6 months as defined by modified National Institutes of health (NIH) Consensus Response Criteria – analysed by the number and proportion of patients in each response category (GvHD) reported within 6 months and overall, as a proportion of the total number of patients recruited with 95% confidence intervals.

Secondary outcome measures
1. Best organ level response (GvHD) as determined by the incremental improvement and changes in individual organ systems involved in cGvHD according to modified NIH Consensus Response Criteria – analysed by the number of patients in each clinical response category (GvHD) based on their overall 'best' response and changes in the patients' organ systems will be reported and presented as a proportion of the total number of patients recruited with 95% confidence intervals within 6 months
2. Quality of Life is measured using the FACT-BMT (version 4) questionnaire at baseline, cycles 1-6 and if clinical response seen cycles 7-10, end of treatment visit and 3 and 6 month follow-up
3. Duration of response measured via average duration of response reported with full range and Reduction in corticosteroid dosage – analysed by the percentage change from baseline in corticosteroid dosage at 6 months and one year

Overall study start date
21/12/2012

Completion date
29/12/2022

Eligibility

Key inclusion criteria
1. Patients with moderate or severe cGvHD OR progressive, recurrent or delayed -onset acute GvHD as defined by the NIH Consensus Conference Diagnostic Criteria who have failed therapy with corticosteroids (+/- calcineurin inhibitors).
Failure of corticosteroid is defined as either:
1.1. Progression of cGvHD on 1 mg/kg/day prednisolone over 2 weeks
1.2. Stable cGvHD on ≥0.5 mg/kg/day prednisolone over 4 weeks
1.3. Inability to taper prednisolone below 0.5mg/kg/day without recurrence of clinical manifestations
1.4. Inability to tolerate first line therapy* (eg steroid myopathy, calcineurin inhibitor-induced renal toxicity)
*Patients must have proven steroid toxicity to meet this criterion for having failed corticosteroid therapy. These cases must be discussed with the Chief Investigator prior to trial entry.

2. Patients must be unable to receive treatment with extracorporeal photophoresis (ECP) therapy (either refractory/intolerant to ECP, lack of ECP availability at local institution or patient /physician preference)
3. Age ≥16 years of age
4. Life expectancy of at least 3 months with no imminent relapse expected
5. Women of childbearing potential and all men must be using adequate birth control measures throughout the study and for a minimum of 3 months following the end of trial treatment
6. Able to provide written informed consent
7. Patients must be able to comply with all study procedures

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 35; UK Sample Size: 35

Total final enrolment
14

Key exclusion criteria
1. Uncontrolled infection ≥ grade 3 requiring treatment at study entry
2. Neutrophil count <1x109/L (support with GCSF permitted)
3. Platelet count <30 x109/L
4. Known HIV infection
5. Known hepatitis B or C
6. ECOG ≥ 3
7. Patients with ocular GvHD only
8. Pulmonary GvHD
9. Patients receiving active therapy for cGvHD within 14 days of study entry (with the exception of corticosteroids and calcineurin inhibitors)
10. Any investigational agents within 14 days of study entry
11. Treatment with ECP within 6 months of study entry
12. Known hypersensitivity to azacitidine
13. Women who are pregnant or breastfeeding
14. Any other condition that in the Investigator's opinion will affect the patient's participation in this trial

Date of first enrolment
29/04/2016

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
England

United Kingdom

Wales

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

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

Study participating centre
Cambridge Cancer Trials Centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrooke's Hospital
Cambridge Biomedical Campus
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CB2 0QQ

Study participating centre
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L7 8XP

Study participating centre
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Becket Street

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LS9 7TF

Study participating centre
University Hospital Wales
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Sponsor type
University/education

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

Publication and dissemination plan
The results of this trial will be submitted for publication in a peer reviewed journal. This would be at the end of the follow-up period (December 2019). Short communications and abstracts may be prepared during the earlier parts of the study depending on the data collected.

Intention to publish date
29/12/2023

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2.0	07/10/2015	21/11/2016	No	Yes
Plain English results			04/05/2022	No	Yes
Interim results article	Results of first stage (tolerability) of two-stage study	01/12/2021	18/12/2023	Yes	No