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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	[ ] Prospectively registered [ ] Protocol
Registration date 21/11/2016	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 18/12/2023	**Condition category** Cancer	[ ] 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

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2014-005659-19

Protocol serial number
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

Primary study design
Interventional

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

Study type(s)
Treatment

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(s)
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.

Key secondary outcome(s)
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 Years

Sex
All

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
United Kingdom

England

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
Hills Road
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CB2 0QQ

Study participating centre
Churchill Hospital
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OX3 7LJ

Study participating centre
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Praed Street
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Study participating centre
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Oxford Road
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Study participating centre
St James University Hospital
Becket Street
Leeds
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LS9 7TF

Study participating centre
University Hospital Wales
Heath Park
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CF14 4XW

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 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?
Interim results article	Results of first stage (tolerability) of two-stage study	01/12/2021	18/12/2023	Yes	No
Participant information sheet	version V2.0	07/10/2015	21/11/2016	No	Yes
Plain English results			04/05/2022	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes