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Phase II study of the tolerability and efficacy of the histone deacetylase inhibitor sodium valproate administered in conjunction with 5-azacitidine, theophylline and all trans-retinoic acid in patients with acute myeloid leukaemia and high risk myelodysplasia

Submission date 21/08/2006	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 05/10/2006	**Overall study status** Completed	
Last Edited 09/05/2012	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HM2009

Study information

Scientific Title

Acronym
Val/Aza

Study objectives
The purpose of this study is to assess the tolerability and anti-leukaemic activity of four drugs, sodium valproate, 5-azacitidine, theophylline and All Trans-Retinoic Acid (ATRA) when administered in combination to patients with Acute Myeloid Leukaemia (AML) or high risk Myelodysplasia (MDS). All four drugs have been shown to have anti-leukaemic activity in vitro but their combined use has not been studied clinically in patients with leukaemia. This study will also analyse the impact of these agents on biochemical measures of chromatin structure and cellular differentiation permitting correlation of these parameters with clinical activity of these drugs in AML and high risk MDS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Midlands multi-centre Research Ethics Committee (reference 05/MRE07/74).

Study design
Phase II, multi-centre, open label, non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Acute myeloid leukaemia or high risk myelodysplasia

Interventions
Patients will receive combination therapy with sodium valproate, 5-azacitidine, theophylline and ATRA for the duration of the study (85 days).

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Sodium valproate, 5-azacitidine, theophylline and all trans-retinoic acid.

Primary outcome measure
1. Assessment of safety of the four drugs sodium valproate, 5-azacitidine, theophylline and ATRA when administered in combination
2. Haematological responses to sodium valproate, 5-azacitidine, theophylline and ATRA when administered in combination

Secondary outcome measures
1. To assess the impact of the combined therapy on measures of apoptosis and differentiation
2. To assess the impact of the combined therapy on the chromatin structure of blast cell population

Overall study start date
22/06/2006

Completion date
01/06/2008

Eligibility

Key inclusion criteria
1. Patients satisfying World Health Organisation (WHO) criteria for diagnosis of AML or high risk MDS
2. Relapsed or refractory AML who are considered unfit for intensive chemotherapy
3. Patients with de novo AML who are either older than 70 years, or between 60 and 69 years of age with a history of cardiac disease
4. Patients with high risk MDS judged to be ineligible for intensive chemotherapy or stem cell transplantation
5. Age equal or greater than 18 years
6. WHO performance status of zero to two
7. Patients must be able to swallow capsules
8. At least two weeks from previous chemotherapy
9. Patients with White Blood Cell (WBC) count of more than 15 x 10^9/L may receive Hydroxyurea in order to keep the WBC less than 10 x 10^9/L
10. All men and women must agree to practice effective contraception during the entire study period
11. All women of child bearing potential must have a negative pregnancy test

12. Aspartate transaminase less than or equal to 2.5 x the Upper Limit of Normal (ULN)
13. Total bilirubin less than or equal to 2.5 x the ULN
14. Calculated creatinine clearance more than or equal to 50 mL/minute
15. Written informed consent, and the ability of the patient to co-operate with treatment and follow up must be ensured and documented

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
20

Key exclusion criteria
1. Patients with contraindications to receiving sodium valproate, ATRA or 5-azacitidine will be excluded from the study. Contraindications are detailed as follows:
a. sodium valproate - hypersensitivity to sodium valproate, acute liver disease, family history of severe hepatic dysfunction, porphyria, history of pancreatitis, active systemic lupus erythematosis
b. ATRA - hypersensitivity to ATRA
c. 5-azacitidine - hypersensitivity to 5-azacitidine
d. history of sensitivity to theophylline
2. Patients who are high medical risks because of non-malignant systemic disease, as well as those with active uncontrolled infection
3. Patients with any other condition which in the investigator's opinion would not make the patient a good candidate for the clinical trial
4. Pregnant or lactacting women
5. Patients known to be serologically positive for Hepatitis B, C or Human Immunodeficiency Virus (HIV)
6. Concurrent congestive heart failure or prior history of New York Heart Association class III/IV cardiac disease

Date of first enrolment
22/06/2006

Date of final enrolment
01/06/2008

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2TH

Sponsor information

Organisation
University of Birmingham (UK)

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Sponsor type
University/education

Website
http://www.bham.ac.uk

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Industry

Funder Name
Pharmion Ltd (UK)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	16/09/2010		Yes	No