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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

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

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

**Contact name**
Prof Charles Craddock

**Contact details**
Queen Elizabeth Hospital
Centre for Clinical Haematology
Edgbaston
Birmingham
United Kingdom
B15 2TH

## Additional identifiers

**Protocol serial number**
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

## Study type(s)
Treatment

## 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(s)

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

### Key secondary outcome(s)
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

### 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

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 years

### Sex

All

### 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
United Kingdom

England

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

## Sponsor information

### Organisation
University of Birmingham (UK)

### ROR

https://ror.org/03angcq70

# Funder(s)

**Funder type**
Industry

**Funder Name**
Pharmion Ltd (UK)

# Results and Publications

## 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 |