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Leukaemia Lymphoma Research and NCRI Working Group Pick a Winner Programme (LI-1) Trial

Submission date 29/11/2010	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 14/03/2011	**Overall study status** Completed	
Last Edited 04/10/2021	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-sapacitabine-AC220-vosaroxin-cytarabine-acute-myeloid-leukaemia-aml-li-1

Study website
http: amlpaw.cf.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2011-000749-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 1, November 2010

Study information

Scientific Title
Leukaemia Lymphoma Research and NCRI Working Group Pick a Winner Programme (LI-1) Trial
Trial: Multicentre phase II/III interventional study

Acronym
LI-1

Study objectives
Standard care treatment for Acute Myeloid Leukaemia (AML) patients over the age of 60 not fit for intensive chemotherapy may be improved upon either in combination with novel agents or by use of novel agents alone

Ethics approval required
Old ethics approval format

Ethics approval(s)
LI-1 is being submitted to MREC for Wales in December 2010 or January 2011

Study design
Multicentre phase II/III interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Acute myeloid leukemia (AML) patients over 60

Interventions

The following treatments will be compared
1. Low dose Ara-C (cytarabine): 20 mg twice a day (b.i.d) by subcutaneous injection daily on days 1-10 (20 doses) to be repeated at 28 to 42 day intervals.
2. Sapacitabine: 300mg orally b.i.d. for 3 consecutive days in week one and in week two. This should be followed by a minimum of 4 weeks of no treatment. This comprises one course.
3. Vosaroxin: Intravenous infusion in a dose of 72mg/m2 over 10 minutes on days 1 and 4 of each treatment course (two doses).
4. Low dose Ara-C + Vosaroxin: as above
5. Low dose Ara-C + AC220: Ara-C as above plus AC220 oral solution at allocated dose (135mg or 90mg or 60mg) once a day on an empty stomach at least 1 hour before or 2 hours after a meal in the morning for 21 consecutive days as 1 cycle of treatment.
6. 'Other novel agent'

Recruitment will proceed until at least 50 patients have entered each comparative arm (Ara-C and novel therapy). For treatments where the proposed effect is to improve survival by inducing a greater number of remissions, this component will then be analysed using complete remission as the measure.

Patients will be expected to receive four courses of treatment and are followed up annually for life.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Ara-C (cytarabine), sapacitabine, vosaroxin, quizartinib (AC220), tosedostat (CHR-2797)

Primary outcome measure
1. Overall survival
2. Complete remission (CR + CRi) achievement and reasons for failure (for induction questions) assessed locally via bone marrow samples (as per standard care) after each course
3. Duration of response (CR, CRi) relapse rates and deaths in first CR
4. Toxicity, both haematological and non-haematological
5. Supportive care requirements (and other aspects of health economics)
6. Quality of Life Assessment

Secondary outcome measures
1. Presence of a cytogenetic abnormality in the bone marrow of patients in morphological remission
2. Molecular characteristics and response to treatment

Overall study start date
01/04/2011

Completion date
01/01/2020

Eligibility

Key inclusion criteria
1. Patients have one of the forms of acute myeloid leukaemia, except Acute Promyelocytic Leukaemia as defined by the WHO Classification (Appendix A) this can be any type of de novo or secondary AML or high risk Myelodysplastic Syndrome, defined as greater than 10% marrow blasts (RAEB-2)
2. Normally over the age of 60, but patients under this age are eligible if they are not considered fit for the NCRI AML16 trial or any subsequent equivalent trial
3. Written informed consent
4. For the AC220 interventions cardiac criteria must be met. Electrolyte levels of potassium, magnesium and calcium must be within the institutional normal range

Participant type(s)
Patient

Age group
Senior

Sex
Both

Target number of participants
1000

Total final enrolment
243

Key exclusion criteria
1. Patients have previously received cytotoxic chemotherapy for AML. (Hydroxycarbamide or similar low-dose therapy, to control the white count is not an exclusion criterion)
2. For AC220 treatment the following criteria make a patient ineligible for that randomisation:
2.1. A myocardial infarction within 12 months
2.2. Uncontrolled angina within 6 months
2.3. Current or history of congestive heart failure New York Heart Association (NYHA) class 3 or 4, unless an echocardiogram (ECHO) or multiple gated acquisition scan (MUGA) performed either within 1 month prior to study screening or during screening results in a left ventricular ejection fraction (LVEF) that is ≥ 45% (or institutional lower limit of normal value)
2.4. Diagnosed or suspected congenital long QT syndrome. Any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, torsades de pointes [TdP]) or any history of arrhythmia will be discussed with the clinical coordinator/safety physician prior to patients entry into the study
2.5. Prolonged QTcF interval on pre-entry ECG (≥450 ms)
2.6. Any history of second or third degree heart block (may be eligible if the patient currently has a pacemaker
2.7. Heart rate < 50/minute on pre-entry ECG
2.8. Uncontrolled hypertension
2.9. Obligate need for a cardiac pacemaker
2.10. Complete left bundle branch block
2.11. Atrial fibrillation
3. In blast transformation of chronic myeloid leukaemia (CML)
4. Concurrent active malignancy under treatment

5. Pregnant or lactating
6. Acute Promyelocytic Leukaemia
7. Known infection with human immunodeficiency virus (HIV)

Date of first enrolment
01/04/2011

Date of final enrolment
01/01/2019

Locations

Countries of recruitment
Australia

Denmark

France

United Kingdom

Wales

Study participating centre
Department of Haematology,
Cardiff
United Kingdom
CF14 4XN

Sponsor information

Organisation
Cardiff University (UK)

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Other

Funder Name
Leukaemia and Lymphoma Research (LLR) (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
Cardiff University (UK)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

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 for combination of low-dose ara-C plus tosedostat versus low-dose ara-C alone	01/07/2021	10/05/2021	Yes	No
Results article	Results for combination of low-dose ara-C plus quizartinib versus low-dose ara-C alone	01/10/2021	04/10/2021	Yes	No