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Single agent pegylated arginine deiminase (ADI-PEG 20) in patients with malignant pleural mesothelioma

Submission date 12/10/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 12/10/2010	**Overall study status** Completed	
Last Edited 26/10/2018	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-study-looking-new-drug-treat-mesothelioma-adam

Study website
http://www.cancer.qmul.ac.uk/staff/szlosarek.html

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT01279967

Secondary identifying numbers
006836

Study information

Scientific Title
A randomised stratified multicentre phase II clinical trial of single agent pegylated arginine deiminase (ADI-PEG 20) in patients with malignant pleural mesothelioma

Acronym
ADAM

Study objectives
Mesothelioma is a profoundly apoptosis resistant malignancy with the benefit of palliative chemotherapy confined to a subgroup of patients (less than 40%). The rationale underlying arginine depletion with ADI-PEG 20 is that arginine auxotrophic tumours undergo programmed cell death or apoptosis, due to an absence of the rate-limiting enzyme for arginine biosynthesis, ASS1. We have documented that ASS1 is commonly absent in patients with malignant pleural mesothelioma (MPM) and that ADI-PEG 20 induces apoptosis of ASS1 negative MPM tumours. This study seeks to define the role of ADI-PEG 20 in patients with confirmed ASS1-negative MPM, whilst avoiding the known difficulties inherent in MPM response assessments, with a best supportive care control arm. Patients who are either not keen or unfit for front-line chemotherapy, will be randomised into this window study.

The main purpose of this study is to look at the effectiveness of ADI-PEG 20 at controlling mesothelioma in patients who do not receive chemotherapy. We will also compare the results with patients who receive best supportive care only.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The South East research Ethics committee, South East Coast Strategic Health Authority on 30/12 /2009 (ref: 09/H1102/107). Amendments approved on 06/07/2010 and 04/10/2010.

Study design
Randomised stratified multicentre phase II clinical trial

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 contact ADAM study Coordinator, Li-Hui Chen (adam@qmcr.qmul.ac.uk) to request a patient information sheet

Health condition(s) or problem(s) studied
Malignant pleural mesothelioma

Interventions
Patients with ASS1-negative mesothelioma confirmed by immunohistochemistry will be randomised as follows:
Arm A: Best supportive care (n = 21)
Arm B: ADI-PEG 20 and best supportive care (n = 42)

Assessment of tumoural ASS1 status by immunohistochemistry and a baseline PET-CT will take place. Patients randomised to Arm B will receive a weekly intramuscular injection of ADI-PEG 20 and weekly routine blood tests, PD and PK bloods. A repeat PET-CT will be performed between week 3 and 4 on the protocol for patients in Arm B. All patients (Arm A and B) will be followed up on a regular basis with a CT scan every 2 months. Monthly bloods and urine collection for translational research. A repeat tumoural biopsy on progression in a patient with an initial response to ADI-PEG 20.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Pegylated arginine deiminase (ADI-PEG 20)

Primary outcome measure
Progression-free survival, measured from the date of randomisation until the date of progression or death, whichever occurs first.

Secondary outcome measures
1. Response rate, measured by image assessment every two months
2. Median overall survival
3. Toxicity, measured continuously throughout the study

Overall study start date
01/01/2010

Completion date
21/05/2013

Eligibility

Key inclusion criteria
1. Males and females aged 18 years and older (there is no upper age limit)
2. Histopathological evidence of ASS-negative MPM. All biopsies will be reviewed for ASS expression using immunohistochemistry (central review by Dr Michael Sheaff, Institute of Cell and Molecular Sciences, Barts and The London School of Medicine)
3. Performance status Eastern Cooperative Oncology Group (ECOG) 0 - 1
4. No prior systemic chemotherapy
5. Computed tomography (CT) evaluable disease by modified Response Evaluation Criteria in Solid Tumours (RECIST) criteria
6. Adequate haematological status (haemoglobin 10 g/dl or greater; white cell count 2 x 10^9/L or greater, neutrophil count 1.5 x 10^9/L or greater; platelets 100 x 10^9 /L or greater)
7. Adequate hepatic function (bilirubin less than 1.5 x upper limit of normal; aspartate aminotransferase (AST) and alanine aminotransferase (ALT) less than 3 x upper limit of normal)
8. Creatinine clearance greater than 30 ml/min
9. Willing to give written informed consent to participate

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
63

Key exclusion criteria
1. Any of the above inclusion criteria are not met
2. Enrolment in another clinical trial
3. Patients with surgically resectable disease
4. Recurrent pleural effusion (not pleurodesed)
5. Receipt of extensive radiation (hemi-thorax) therapy within 6 weeks before enrolment. Radiation to chest port sites following thoracotomy is permitted.
6. A history of prior malignant tumour, unless the patient has been without evidence of disease for at least three years, or the tumour was a non-melanoma skin tumour or in-situ cervix carcinoma
7. Symptomatic or known brain or leptomeningeal metastases
8. Uncontrolled or severe cardiovascular disease including myocardial infarction within 6 months of enrolment
9. New York Heart Association (NYHA) class III or IV heart failure (attachment 10, NYHA Classification of Cardiac Disease), uncontrolled angina, clinically significant pericardial disease, or cardiac amyloidosis
10. Serious medical (e.g. uncontrolled diabetes, hepatic disease, infection) or psychiatric illness likely to interfere with participation in this clinical study
11. History of seizures
12. Patients of child-bearing age must not become pregnant. Females of childbearing potential

must have a negative pregnancy test within 7 days prior to being registered for protocol therapy. Acceptable birth control measures whilst on the study include barrier and hormonal methods; patients that are surgically sterile are also eligible to participate in this study.
13. Females must not be breastfeeding
14. Prior exposure to ADI-PEG 20
15. Pre-planned surgery or procedures that would interfere with the study protocol
16. Allergy to pegylated products

Date of first enrolment
02/03/2011

Date of final enrolment
21/05/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Mary University of London
London
United Kingdom
EC1M 6BQ

Sponsor information

Organisation
Barts and The London NHS Trust (UK)

Sponsor details
Mr Gerry Leonard
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E1 2EF

Sponsor type
Hospital/treatment centre

Website
http://www.bartsandthelondon.nhs.uk/research/

ROR
https://ror.org/00b31g692

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) - (ref:C12522/A7740)

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

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?
Plain English results				No	Yes
Results article	results	01/01/2017		Yes	No
HRA research summary			28/06/2023	No	No