

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

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

Plain English summary of protocol

<http://www.cancerhelp.org.uk/trials/a-study-looking-new-drug-treat-mesothelioma-adam>

Contact information

Type(s)

Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)

NCT01279967

Protocol serial number

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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 $2 \times 10^9/L$ or greater, neutrophil count $1.5 \times 10^9/L$ or greater; platelets $100 \times 10^9/L$ 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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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**

United Kingdom

England

Study participating centre
Queen Mary University of London
London
United Kingdom
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Sponsor information

Organisation
Barts and The London NHS Trust (UK)

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, Cancer Research UK (CRUK), CRUK

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

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2017		Yes	No
HRA research summary			28/06/2023	No	No
Plain English results				No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes