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DIAPHRAGM: Diagnostic and prognostic biomarkers in the rational assessment of mesothelioma

Submission date 03/10/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol
Registration date 17/10/2013	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 20/10/2017	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/a-study-looking-blood-tests-diagnose-mesothelioma-diaphragm

Contact information

Type(s)
Scientific

Contact name
Dr Kevin Blyth

Contact details
Consultant Respiratory Physician & Honorary Senior
Clinical Lecturer
Department of Respiratory Medicine
Southern General Hospital
1345 Govan Road
Glasgow
United Kingdom
G51 4TF
+44 (0)141 232 4026
kevin.blyth@ggc.scot.nhs.uk

Additional identifiers

Protocol serial number
DIAPHRAGM-2013

Study information

Scientific Title
DIAPHRAGM study: to prospectively assess whether the levels of two novel biomarkers (SOMAscan and Fibulin-3) in blood, can distinguish between malignant pleural mesothelioma (MPM), other malignant pleural effusions and from people who have had previous exposure to asbestos but have no evidence of MPM

Acronym
DIAPHRAGM

Study objectives
Novel biomarkers are urgently required for the diagnosis, prognostication and monitoring of MPM. An ideal MPM biomarker would be measurable in blood, have sufficient sensitivity and specificity for MPM to improve diagnostic accuracy in patients presenting with a pleural effusion, provide useful prognostic/monitoring information in patients with confirmed MPM and clinicians would have a clear understanding of the biological basis of the information provided.

We hypothesise that SOMAscan and/or Fibulin-3 will provide clinically useful diagnostic /prognostic information regarding MPM when these biomarkers are measured in blood, in patients presenting with suspected pleural malignancy.

The primary aim is to determine whether levels of SOMAscan and/or Fibulin-3 in blood at presentation can differentiate MPM from asbestos-exposed controls and patients with other causes of pleural effusion with sufficient degree of sensitivity and specificity to be of routine clinical value.

Secondary aims are:
1. Determine whether levels of SOMAscan and/or Fibulin-3 at presentation provide clinically useful prognostic information in MPM patients
2. Determine whether early changes in SOMAscan and/or Fibulin-3 levels after diagnosis (defined by a change in levels at 3 months) are associated with a poorer prognosis in MPM.

Exploratory Aims:
1. Determine whether there is any correlation between SOMAscan and/or Fibulin-3 levels in blood and tumour volume, defined by contrast-enhanced Magnetic Resonance Imaging
2. Determine whether there is any correlation between SOMAscan and/or Fibulin-3 levels in blood and tumour angiogenesis (defined by redistribution rate constant (Kep) and elimination rate constant (Kel)) on contrast-enhanced magnetic resonance (MR) imaging
3. Determine whether there is any correlation between SOMAscan and/or Fibulin-3 levels in blood and pleural fluid at presentation in patients with MPM
4. Determine whether SOMAscan and/or Fibulin-3 levels are affected by pleural fluid drainage and pleurodesis at the time of diagnosis

Ethics approval required
Old ethics approval format

Ethics approval(s)
West of Scotland REC 1; REC Ref: 13/WS/0240, approval pending

Study design

Prospective multi-centre observational study incorporating a nested cross-sectional sub-study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Suspected pleural malignancy or documented history of asbestos exposure

Interventions
Patients with suspected pleural malignancy:
Visit 1 (Day 0, first clinic visit or in patient stay at hospital)
Core Study Activity:
1. Asbestos exposure history
2. Review eligibility criteria
3. Introduce to study if eligibility criteria met
4. Provide with Core Study Patient Information Sheet (at clinic or via post)

Visit 2 (Day 3)
Core Study Activity:
1. Opportunity for discussion regarding study
2. Sign core study consent form
3. Register patient with Clinical Trials Unit
4. ECOG Performance Status
5. Blood draw for biomarkers with appropriate processing and storage
6. Asbestos exposure history (if not previously performed)
7. Record baseline prognostic indicators, including haemoglobin, leucocyte and platelet counts, lactate dehydrogenase, c-reactive protein and albumin

Visit 3 (Day 9)
Core Study Activity:
1. If a diagnosis of MPM is made - enter follow-up
2. If any non-MPM diagnosis made - exit study

MRI sub-study activity
If no diagnosis is made - consider MRI sub-study (only in WOS patients)
1. Review sub-study eligibility criteria
2. Introduce sub-study if eligible
3. Provide with separate sub-study PIS
4. MRI Safety Questionnaire
5. X-ray orbits if any history of eye injury and retained metallic foreign body

Visit 3a (Day 11-18)

Core Study Activity: None

MRI sub-study activity
1. Opportunity for further discussion with CRF
2. MRI Safety Questionnaire (if not previously recorded)

3. Sign sub-study Consent From
4. Register subject with CTU
5. Pleural MRI scan

Visit 4 (Day 14-21)

Core Study Activity:
No activity

MRI sub-study activity
Paired Blood and Pleural Fluid Draw for biomarkers with appropriate processing and storage

Visit 5 (day 23-31)
Core Study Activity:
1. If diagnosis of MPM made - enter follow-up
2. If non-MPM diagnosis made - exit study

MRI sub-study activity: None

Visit 6 (Day 62)
Core Study Activity:
Blood draw for SOMAscan and Fibulin-3

MRI sub-study activity: None

Visit 7 (Day 123)
Core Study Activity:
Blood draw for SOMAscan and Fibulin-3

MRI sub-study activity: None

Follow Up Assessment
Core Study Activity:
Two monthly follow up assessments to be performed to determine survival status and any cancer treatments delivered

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. SOMAscan and Fibulin-3 in blood at presentation
2. Final diagnosis reached

Key secondary outcome(s))
1. SOMAscan and Fibulin-3 levels at presentation and at 3 months
2. Survival

Exploratory Research Outcomes
1. Correlation between SOMAscan and/or Fibulin-3 levels and tumour volume, defined by

planimetry at contrast-enhanced Magnetic Resonance Imaging
2. Correlation between SOMAscan and/or Fibulin-3 levels and tumour angiogenesis, Redistribution rate constant (Kep) and elimination rate constant (Kel)) on contrast-enhanced magnetic resonance (MR) imaging
3. SOMAscan and Fibulin-3 in paired blood and pleural fluid samples
4. SOMAscan and Fibulin-3 levels at presentation and at 1 month post-biopsy and pleurodesis

Completion date
31/10/2016

Eligibility

Key inclusion criteria
Cases of suspected pleural malignancy:
1. Informed written consent
2. Suspected pleural malignancy, as defined by a unilateral pleural effusion or pleural-based mass lesion
3. Sufficient fitness for diagnostic sampling, including diagnostic pleural aspiration as a minimum
4. Aged over 18

Patients with suspected pleural malignancy recruited to the cross-sectional sub-study will be subject to the following additional inclusion criteria:
1. Recruited in a WoS centre (Southern General, Gartnavel General, Glasgow Royal)
2. Thoracoscopy indicated to investigate suspected pleural malignancy (defined by negative pleural cytology and non-specific CT findings)
3. Aged over 18

Asbestos-exposed subjects:
1. Documented history of asbestos exposure and associated pleural plaques, asbestosis or diffuse pleural thickening
2. Informed written consent
3. Willing and able to travel to a research clinic interview in Glasgow
4. Aged over 18

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

Cases of suspected pleural malignancy:
1. Insufficient fitness (based on the site investigators clinical judgement) for diagnostic sampling, including diagnostic pleural aspiration as a minimum

Patients with suspected Pleural Malignancy recruited to the cross-sectional sub-study will be subject to the following additional exclusion criteria:
1. Claustrophobia
2. Pregnancy
3. Unable to undergo MR imaging due to known contraindications (e.g. pacemaker, ferrous metal implants or foreign body)
4. Allergy to Gadolinium contrast
5. Renal impairment (eGFR <30ml/min)

Asbestos-exposed subjects:
1. Known MPM
2. Known pleural effusion of any cause

Date of first enrolment
01/11/2013

Date of final enrolment
31/10/2016

Locations

Countries of recruitment
United Kingdom

Scotland

Ireland

Study participating centre
Southern General Hospital
Glasgow
United Kingdom
G51 4TF

Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Government

Funder Name
Chief Scientist Office (UK) Ref: ETM/285

Alternative Name(s)
CSO

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

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?
Protocol article	protocol	24/11/2016		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes