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Mesothelioma and Radical Surgery 2

Submission date
23/08/2018

Recruitment status
No longer recruiting

Registration date
05/09/2018

Overall study status
Completed

Last Edited
27/09/2024

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-surgery-for-mesothelioma-mars-2

Current plain English summary as of 29/08/2019:
Background and study aims
Mesothelioma is a cancer of the thin membrane that lines the chest. Around 2500 people in the UK are diagnosed with mesothelioma each year. Exposure to asbestos is the most common cause, although the cancer does not usually become apparent until 40-60 years after exposure. Anti-cancer drugs (chemotherapy) are usually given to help treat mesothelioma and sometimes lung-sparing surgery (pleurectomy decortication) is undertaken. However, it is not known if this surgery, in addition to chemotherapy, can increase survival and improve the quality of life for patients. The aim of this study (MARS 2) study is to compare combining this surgery and chemotherapy with chemotherapy alone with respect to overall survival, cost-effectiveness and quality of life at regular intervals for at least 2 years.

Who can participate?
Adults over the age of 16 who have been diagnosed with malignant pleural mesothelioma

What does the study involve?
We would like to assess whether surgery offers any benefit or not over standard clinical care in terms of improving survival and quality of life. Patients deemed suitable for surgery will be approached and participants will receive 2 cycles of chemotherapy and a computed tomography (CT) scan. If there is no significant worsening of cancer, participants will be randomly allocated to either surgery and up to 4 further cycles of chemotherapy or no-surgery and up to 4 further cycles of chemotherapy. All patients in the study will be closely monitored at several follow-up time points (6 weeks, 6 months, 12 months, 18 months and 24 months, and then at 6-monthly intervals until the end of the study) that will be scheduled after allocation to one of the study groups. At each of these time points up to 24 months patients will receive a phone call from the research team and be asked to complete some more quality of life questionnaires. After 24 months, patient will be sent a questionnaire, at 6-monthly intervals, to ascertain any new diagnoses and additional therapy received. MARS 2 also includes an Information study, where patients may be interviewed or have their consultations audio-recorded if they are happy with this. The aim of the Information study is to explore how a patient makes a decision to take part in research or not, with the overall aim of improving recruitment to clinical trials.

What are the possible benefits and risks of participating?
Participants may not personally gain any benefit from taking part in this study. The information we get from this study may help doctors decide how to treat malignant pleural mesothelioma in the future and how research is discussed with future patients.

Where is the study run from?
The MARS 2 study is being coordinated by the Clinical Trials and Evaluation Unit (CTEU) at the University of Bristol. There are currently 26 centres taking part in MARS 2.

When is the study starting and how long is it expected to run for?
February 2013 to September 2022

Who is funding the study?
National Institute for Health Research - Health Technology Assessment Programme (15/188/31) (UK)

Who is the main contact?
Prof. Eric Lim
e.lim@rbht.nhs.uk

Previous plain English summary:
Background and study aims
Mesothelioma is a cancer of the thin membrane that lines the chest. Around 2500 people in the UK are diagnosed with mesothelioma each year. Exposure to asbestos is the most common cause, although the cancer does not usually become apparent until 40-60 years after exposure. Anti-cancer drugs (chemotherapy) are usually given to help treat mesothelioma and sometimes lung-sparing surgery (pleurectomy decortication) is undertaken. However, it is not known if this surgery, in addition to chemotherapy, can increase survival and improve the quality of life for patients. The aim of this study (MARS 2) study is to compare combining this surgery and chemotherapy with chemotherapy alone with respect to overall survival, cost-effectiveness and quality of life at regular intervals for 2 years.

Who can participate?
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We would like to assess whether surgery offers any benefit or not over standard clinical care in terms of improving survival and quality of life. Patients deemed suitable for surgery will be approached and participants will receive 2 cycles of chemotherapy and a computed tomography (CT) scan. If there is no significant worsening of cancer, participants will be randomly allocated to either surgery and 4 further cycles of chemotherapy or no-surgery and 4 further cycles of chemotherapy. All patients in the study will be closely monitored at several follow-up time points (6 weeks, 6 months, 12 months, 18 months and 24 months) that will be scheduled after allocation to one of the study groups. At each of these time points they will receive a phone call from the research team and be asked to complete some more quality of life questionnaires. MARS 2 also includes an Information study, where patients may be interviewed or have their consultations audio-recorded if they are happy with this. The aim of the Information study is to explore how a patient makes a decision to take part in research or not, with the overall aim of improving recruitment to clinical trials.

What are the possible benefits and risks of participating?
Participants may not personally gain any benefit from taking part in this study. We hope that any

treatments received will help participants, however, this cannot be guaranteed. The information we get from this study may help doctors decide how to treat malignant pleural mesothelioma in the future and how research is discussed with future patients.
The possible risks of taking part include the standard risks of surgery (pain, bleeding and infection). Complications rarely develop after surgery but these can include kidney problems, heart attack and stroke. CT scans are considered safe; however, as with any injection, the injection aspect carries a slight risk of harm, including injury to a nerve, artery or vein, or a reaction to the material being injected. Occasionally, patients have mild reactions to the contrast agent and develop sneezing or hives. The staff of the X-ray department are trained to treat these reactions.

Where is the study run from?
Clinical Trials and Evaluation Unit (CTEU) at the University of Bristol and 22 centres across the UK

When is the study starting and how long is it expected to run for?
February 2013 to March 2023

Who is funding the study?
National Institute for Health Research - Health Technology Assessment Programme (15/188/31) (UK)

Who is the main contact?
Prof. Eric Lim
e.lim@rbht.nhs.uk

Study website
http://cteu.bris.ac.uk/our-studies/?trialType=Thoracic-surgery#5202

Contact information

Type(s)
Scientific

Contact name
Prof Eric Lim

Contact details
Royal Brompton Hospital
Sydney Street
London
United Kingdom
SW3 6NP
0207 351 8591
e.lim@rbht.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT02040272

Secondary identifying numbers
15/188/31

Study information

Scientific Title
Mesothelioma and Radical Surgery 2: a multicentre randomised trial comparing (extended) pleurectomy decortication versus no (extended) pleurectomy decortication for patients with malignant pleural mesothelioma.

Acronym
MARS 2

Study objectives
(Extended) pleurectomy decortication and chemotherapy is superior to chemotherapy alone with respect to overall survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Camberwell St Giles Research Ethics Committee, 28/10/2017, REC ref: 13/LO/1481

Study design
Interventional multi-centre open-label parallel two-group pragmatic randomized controlled 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 use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Pleural mesothelioma

Interventions

Current interventions as of 29/08/2019:
Participants will be randomly allocated to either the intervention group or the control group. Randomisation will be carried out electronically using a secure web-based system (Sealed Envelope (https://sealedenvelope.com)). The allocation will not be revealed until sufficient information to uniquely identify the participant has been entered. Minimisation (with a random component) for selected baseline variables (age, performance status and cell type) that influence survival, in addition to stratification by centre to ensure that the cohorts are as balanced as possible, will be applied. Randomisation will be carried out by a member of the research team at the medical centre after the participant has received 2 cycles of chemotherapy, and had a further CT scan to confirm eligibility (i.e. resectable disease).
Participants in both groups will receive an initial 2 cycles of standard chemotherapy (platinum and pemetrexed), which will take around 3 weeks per cycle.

The experimental intervention group will receive chemotherapy and surgery for mesothelioma. Pleurectomy decortication surgery involves removal of the lining of the chest wall and lining of the lung, possibly also with the sac around the heart and/or diaphragm ("extended") as required to achieve complete tumour removal but leaving the lung in-situ. The decision to perform pleurectomy decortication or extended pleurectomy decortication will be made by the surgeon based on surgical findings. Patients in this group will usually be in hospital for approximately 10-14 days, and the post-operative recovery period is usually 3 weeks. Participants will then receive up to 4 cycles of platinum and pemetrexed chemotherapy.

The control group will receive a further 4 cycles of the standard chemotherapy above.

Participants in both groups will be followed up after 6 weeks, and 6, 12, 18 and 24 months, and then every 6 months until the end of the study. Participants who have had surgery will also attend the surgical centre for a post-operative check, usually 3-6 weeks post-surgery.
MARS 2 also includes an Information study called the QuinteT Recruitment Intervention (QRI), which aims to optimise recruitment and informed consent by understanding and addressing recruitment challenges across the centres in a tailored and flexible way. Patients will have the option of having their discussions with health professionals about MARS2 audio-recorded, along with an optional interview with a researcher to understand their perspectives on the study, the treatment offered, and why they made the decision they did. Interviews will also be undertaken with study staff and recruiters, along with scrutiny of screening logs and patient-facing documents. This data will be combined to identify key recruitment challenges. Having identified key difficulties, tailored strategies can then be offered to minimise these, which may include recruiter training, and suggestions to change patient pathways and patient-facing documents. Recruitment rates will be mapped against the timings of strategies and evidence of improvements in informed consent will be sought to indicate evidence of effectiveness.

Previous interventions:
Participants will be randomly allocated to either the intervention group or the control group. Randomisation will be carried out electronically using a secure web-based system (Sealed Envelope (https://sealedenvelope.com)). The allocation will not be revealed until sufficient information to uniquely identify the participant has been entered. Minimisation (with a random component) for selected baseline variables (age, performance status and cell type) that influence survival, in addition to stratification by centre to ensure that the cohorts are as balanced as possible, will be applied. Randomisation will be carried out by a member of the research team at the medical centre after the participant has received 2 cycles of chemotherapy, and had a further CT scan to confirm eligibility (i.e. resectable disease).
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and pemetrexed), which will take around 3 weeks per cycle.
The experimental intervention group will receive chemotherapy and surgery for mesothelioma. Pleurectomy decortication surgery involves removal of the lining of the chest wall and lining of the lung, possibly also with the sac around the heart and/or diaphragm ("extended") as required to achieve complete tumour removal but leaving the lung in-situ. The decision to perform pleurectomy decortication or extended pleurectomy decortication will be made by the surgeon based on surgical findings. Patients in this group will usually be in hospital for approximately 10-14 days, and the post-operative recovery period is usually 3 weeks. Participants will then receive up to 4 cycles of platinum and pemetrexed chemotherapy within 12 weeks of the operation.
The control group will receive a further 4 cycles of the standard chemotherapy above.
Participants in both groups will be followed up after 6 weeks, and 6, 12, 18 and 24 months. Participants who have had surgery will also attend the surgical centre for a post-operative check, usually 3-6 weeks post-surgery.
MARS 2 also includes an Information study called the QuinteT Recruitment Intervention (QRI), which aims to optimise recruitment and informed consent by understanding and addressing recruitment challenges across the centres in a tailored and flexible way. Patients will have the option of having their discussions with health professionals about MARS2 audio-recorded, along with an optional interview with a researcher to understand their perspectives on the study, the treatment offered, and why they made the decision they did. Interviews will also be undertaken with study staff and recruiters, along with scrutiny of screening logs and patient-facing documents. This data will be combined to identify key recruitment challenges. Having identified key difficulties, tailored strategies can then be offered to minimise these, which may include recruiter training, and suggestions to change patient pathways and patient-facing documents. Recruitment rates will be mapped against the timings of strategies and evidence of improvements in informed consent will be sought to indicate evidence of effectiveness.

Intervention Type
Procedure/Surgery

Primary outcome measure
Current primary outcome measure as of 29/08/2019:
Survival up to the end of the study, determined by confirmation of death by the trial site

Previous primary outcome measure:
Survival up to 2 years after randomisation, determined by confirmation of death by the trial site

Secondary outcome measures
Current secondary outcome measures:
1. Progression-free survival to the end of the study (minimum of 2 years after randomisation into the study), assessed by recurrence, which is collected using purpose-designed Case Report Forms and questionnaires at each follow-up appointment (6 weeks and 6, 12, 18 and 24 months after treatment and every 6 months thereafter until the end of the study)
2. Serious adverse health events 2 years after randomisation into the study, collected using purpose-designed Case Report Forms at each follow-up appointment (up to 24 months)
3. Health-related quality of life, assessed after 6 weeks and 6, 12, 18 and 24 months after randomisation into the study using:
3.1. European Organization for Research and Treatment Core Quality of Life Questionnaire (EORTC QLQ-C30)
3.2. EuroQol-5D-5L (EQ-5D-5L)

4. Resource and health service use, collected using purpose-designed Case Report Forms at each follow-up appointment (up to 24 months) and during initial surgical admission for the intervention group

Previous secondary outcome measures:
1. Progression-free survival 2 years after randomisation into the study, assessed by recurrence, which is collected using purpose-designed Case Report Forms at each follow-up appointment (6 weeks and 6, 12, 18 and 24 months after treatment)
2. Serious adverse health events 2 years after randomisation into the study, collected using purpose-designed Case Report Forms at each follow-up appointment
3. Health-related quality of life, assessed after 6 weeks and 6, 12, 18 and 24 months after randomisation into the study using:
3.1. European Organization for Research and Treatment Core Quality of Life Questionnaire (EORTC QLQ-C30)
3.2. EuroQol-5D-5L (EQ-5D-5L)
4. Resource and health service use, collected using purpose-designed Case Report Forms at each follow-up appointment and during initial surgical admission for the intervention group

Overall study start date
21/02/2013

Completion date
30/03/2023

Eligibility

Key inclusion criteria
Patient may enter study if ALL of the following apply:
1. Aged 16 years or older
2. Tissue (cytology or histology) confirmed epithelioid, sarcomatoid or biphasic mesothelioma*
3. Disease confined to one hemi-thorax based on CT assessment
4. Disease deemed surgically resectable**
5. Fit for surgery**
6. Capacity to provide written informed consent to participate in the trial

*The “diagnosis” of mesothelioma is based on cytology and / or histopathology results as reviewed by MDT to be of sufficient certainty to recommend chemotherapy as treatment.
**To be confirmed by a surgeon at a MARS 2 surgical site (added 29/08/2019)

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
328

Total final enrolment
335

Key exclusion criteria
Current inclusion criteria as of 29/08/2019:
Patient may not enter study if ANY of the following apply:
1. Severe shortness of breath (this is defined as an Eastern Cooperative Oncology Group (ECOG) status >= 2, or if lung function tests are performed: pre-operative forced expiratory volume after one second (FEV1) or transfer factor of the lung for carbon monoxide (TLco) less than 20%);
2. Serious concomitant disorder that would compromise participant safety during surgery (e.g. evidence of end organ failure)
3. Severe heart failure (this is defined as NYHA III or IV or if an echocardiogram is performed an ejection fraction less than 30%)
4. End stage kidney failure requiring dialysis
5. Liver failure (e.g. encephalopathy and/or coagulation abnormalities)
6. Prisoner
7. Patient lacks capacity to consent
8. Existing co-enrolment in another interventional clinical trial that aims to improve survival

Previous exclusion criteria:
Patient may not enter study if ANY of the following apply:
1. Severe shortness of breath (Eastern Cooperative Oncology Group (ECOG) status >= 2, pre-operative forced expiratory volume after one second (FEV1) or transfer factor of the lung for carbon monoxide (TLco) less than 20%);
2. Serious concomitant disorder that would compromise participant safety during surgery (e.g. evidence of end organ failure)
3. Severe heart failure (EF less than 30% by echocardiogram)
4. End stage kidney failure requiring dialysis
5. Liver failure (e.g. encephalopathy and/or coagulation abnormalities)
6. Prisoner
7. Patient lacks capacity to consent
8. Co-enrolment in another interventional clinical trial

Date of first enrolment
05/05/2015

Date of final enrolment
10/11/2020

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary,
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Barts Health NHS Trust
Royal London Hospital,
Whitechapel Road,
Whitechapel
London
United Kingdom
E1 1BB

Study participating centre
Cardiff & Vale University Health Board
University Hospital of Wales,
Health Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Road,
Bebington
Wirral
United Kingdom
CH63 4JY

Study participating centre
Colchester Hospital University NHS Foundation Trust
Colchester General Hospital,
Turner Road,
Colchester
Essex

United Kingdom
CO4 5JL

Study participating centre
Derby Teaching Hospitals NHS Foundation Trust
Royal Derby Hospital,
Uttoxeter Road
Derby
United Kingdom
D22 3NE

Study participating centre
Golden Jubilee National Hospital
Beardmore Street
Clydebank
Glagow
United Kingdom
G81 4HX

Study participating centre
Greater Glasgow Health Board
JB Russell House,
Gartnavel Royal Hospital,
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
Leeds Teaching Hospitals NHS Trust
Trust Headquarters,
Beckett Street,
St. James's University Hospital
Leeds
United Kingdom
LS9 7TF

Study participating centre
University Hospital of South Manchester NHS Foundation Trust
Southmoor Road
Manchester

United Kingdom
M23 9LT

Study participating centre
Papworth Hospital NHS Foundation Trust
Papworth Everard
Cambridge
United Kingdom
CB23 3RE

Study participating centre
Peterborough and Stamford Hospitals NHS Foundation Trust
Edith Cavell Campus,
Bretton Gate,
Bretton
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Aneurin Bevan University Health Board
Aneurin Bevan University Local Health Board Headquarters,
Mamhilad,
Park Estate,
Pontypool
Torfaen
United Kingdom
NP4 0YP

Study participating centre
Royal Marsden NHS Foundation Trust
Fullham Road
London
United Kingdom
SW3 6JJ

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Trust Headquarters,
8 Beech Hill Road
Sheffield

United Kingdom
S10 2SB

Study participating centre
South Tees Hospitals NHS Foundation Trust
The James Cook University Hospital,
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
South Tyneside NHS Foundation Trust
Harton Lane
South Shields
United Kingdom
NE34 0PL

Study participating centre
Royal Wolverhampton NHS Trust
New Cross Hospital
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
North Bristol NHS Trust
Trust Headquarters, Southmead hospital, Southmead Road, Westbury on Trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Norfolk & Norwich University Hospitals NHS Foundation Trust
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital, Derriford Road, Crownhill
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Barking, Havering and Redbridge University Hospitals NHS Trust
Queen's Hospital, Rom Valley Way, Romford
Essex
United Kingdom
RM7 0AG

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Guy's Hospital, Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Maidstone and Tunbridge Wells NHS Trust
Maidstone Hospital
Hermitage Lane
Maidstone
United Kingdom
ME16 9QQ

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital Birmingham
Mindelsohn Way

Birmingham
United Kingdom
B15 2GW

Sponsor information

Organisation
Royal Brompton and Harefield NHS Foundation Trust

Sponsor details
Sydney Street
London
England
United Kingdom
SW3 6NP
0207 351 8736
p.pettersson@rbht.nhs.uk

Sponsor type
Hospital/treatment centre

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

ROR
https://ror.org/02218z997

Funder(s)

Funder type
Not defined

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Cancer Research UK

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
The findings will be disseminated by usual academic channels, i.e. presentation at international meetings, as well as by peer-reviewed publications (including a full report to the NIHR-HTA programme) and through patient organisations and newsletters to patients, where available.

Intention to publish date
30/03/2024

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/09/2020	04/09/2020	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	results from a complex recruitment intervention within the Mesothelioma and Radical Surgery 2 (MARS 2) study	16/05/2024	20/05/2024	Yes	No
Plain English results			01/07/2024	No	Yes
		10/05	27/09		

Results article	/2024	/2024	Yes	No