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Local cytoreductive treatments for men with newly diagnosed metastatic prostate cancer in addition to standard of care treatment

Submission date 09/11/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 21/11/2018	**Overall study status** Ongoing	
Last Edited 23/08/2023	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-comparing-different-treatments-for-prostate-cancer-that-has-spread-ip2-alanta

Study website
http://imperialprostate.org.uk/atlanta

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03763253

Secondary identifying numbers

18HH4804

Study information

Scientific Title
Additional Treatments to the Local tumour for metastatic prostate cancer: Assessment of Novel Treatment Algorithms

Acronym
IP2 - ATLANTA

Study objectives
The trialists hypothesise that men with metastatic disease who undergo treatment of the local tumour in the form of either radical therapy (prostatectomy or radiotherapy) or minimally invasive ablative therapy (MIAT), combined with metastases directly therapy, will have improved survival compared to those who receive standard of treatment alone. They will be investigating this newly evolving treatment paradigm in a formal randomised control trial (RCT).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/01/2019, Wales Research Ethics Committee 5 Bangor (Health and Care Research Wales Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB; +44(0)2920 785736; WalesREC5@wales.nhs.uk), ref: 19/WA/0005

Study design
Three-arm unblinded randomized controlled trial using a positive control

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
Prostate cancer; metastatic disease (Any T, Any N, M1+) of any grade, stage or Prostate Specific Antigen (PSA) level

Interventions

Current interventions as of 23/08/2023:
Stratified randomisation via the electronic platform REDCap database.

Intervention Arm 1:
Minimally Invasive Ablative Therapy (MIAT) to prostate in addition to SOC systemic treatment. The exact treatment protocol and modality used (cryotherapy or high intensity focused ultrasound, HIFU) will be set within the MIAT SOP. For those patients who are undergoing MIAT no local prostate radiotherapy will be given as part of the intervention. Radiotherapy can be given subsequently for palliative reasons. MIAT can be provided by a site other than the recruiting site with follow-up visits at recruiting site.

Intervention Arm 2:
Radical therapy (prostatectomy or external beam radiotherapy [Prostate radiotherapy using a dose of external beam radiotherapy of 60Gy/20Fr over 27 days OR 74-78Gy in 2Gy per fraction with or without simultaneous nodal radiotherapy, as defined in Local Radiotherapy SOP]) in addition to SOC systemic treatment. Modality based on physician and patient preference and patient co-morbidities. Radiotherapy or surgery can be provided by a site other than the recruiting site with follow-up visits at the recruiting site. The surgical technique is at the discretion and expertise of the surgical team but will be laid down in the Prostatectomy SOP. For those patients who are undergoing radical prostatectomy no local prostate radiotherapy will be given as part of the intervention. Radiotherapy can be given subsequently for palliative reasons. The radiotherapy doses and protocol in this arm will be higher defined in the Radiotherapy Intervention Arm 2 SOP.

Metastases Directed Therapy (Intervention Arm 1 and 2):
In both intervention arms 1 and 2, metastases directed therapy (MDT) may be used but intent to use MDT to be declared prior to randomisation. In the case of a metastatic recurrence after MDT, a re-treatment with MDT would be allowed if there were new metastatic areas/locations.

The imaging reporting of metastases as well as doses and protocol for MDT as defined in and determined by an Imaging Reporting SOP and a Metastases-Directed Therapy SOP.

Treatment duration of trial therapies: Prostatectomy 1 day; Radiotherapy 4 to 7.5 weeks; Minimally invasive therapy (MIAT) 1 day

[68Ga]PSMA-11 PET-CT Sub study--Now completed:
The trialists will also ask men in the pilot part of ATLANTA if they are willing to undergo a PSMA PET scan. They want to see if this scan might be as accurate in detecting residual disease as prostate biopsies and standard body scans, like MRI, CT or bone scans. This however is optional and participants will be told that they do not have to agree to take part in this optional research, but can still take part in the ATLANTA study. The tests required for this exploratory research will be explained to patients prior to consent in the Patient Information Sheet and verbally by clinician. The target recruitment for this study is 25 patients.

Previous interventions from 08/07/2021 to 23/08/2023:
Stratified randomisation via the electronic platform known as the InForm database.

Intervention Arm 1:
Minimally Invasive Ablative Therapy (MIAT) to prostate in addition to standard of care systemic treatment. The exact treatment protocol and modality used (cryotherapy or high intensity

focused ultrasound, HIFU) will be set within the MIAT SOP. For those patients who are undergoing MIAT no local prostate radiotherapy will be given as part of the intervention. Radiotherapy can be given subsequently for palliative reasons.

Intervention Arm 2:
Radical therapy with either prostatectomy or external beam radiotherapy (high radical dose set out in Radiotherapy Intervention Arm 2 SOP) in addition to standard of care systemic treatment. Modality based on physician and patient preference and patient co-morbidities. The surgical technique is at the discretion and expertise of the surgical team but will be laid down in the Prostatectomy SOP. For those patients who are undergoing radical prostatectomy no local prostate radiotherapy will be given as part of the intervention. Radiotherapy can be given subsequently for palliative reasons.

Metastases Directed Therapy (Intervention Arm 1 and 2):
In both intervention arms 1 and 2, metastases directed therapy (MDT) may be used but intent to use MDT to be declared prior to randomisation. In the case of a metastatic recurrence after MDT, a re-treatment with MDT would be allowed if there were new metastatic areas/locations. The imaging reporting of metastases as well as doses and protocol for MDT will be defined and determined by an Imaging Reporting SOP and a Metastases-Directed Therapy SOP.

In total, 80 men will be approached in 10 UK centre to estimate recruitment rate, acceptability of the trial randomisation, reported toxicities and adherence to trial interventions in a pilot phase- this phase has now been successfully completed. They will also be included into the main phase where 918 will be recruited over 30 UK centres- current phase. Participants will remain in the study for a maximum of 4 years. The aims are to see whether men will participate in this trial (pilot) before a larger trial (main) is run, and the impact of these treatments on quality of life.

[68Ga]PSMA-11 PET-CT substudy:
The trialists will also ask men in the pilot part of ATLANTA if they are willing to undergo a PSMA PET scan. They want to see if this scan might be as accurate in detecting residual disease as prostate biopsies and standard body scans, like MRI, CT or bone-scans. This however is optional and participants will be told that they do not have to agree to take part in this optional research, but can still take part in the ATLANTA study. The tests required for this exploratory research will be explained to patients prior to consent in the Patient Information Sheet and verbally by clinician. Target recruitment for this study is 25 patients. This substudy has now successfully been completed and we are not recruiting into this as we are now in the main phase of the trial.

Previous interventions:
Stratified randomisation via the electronic platform known as the InForm database.

Intervention Arm 1:
Minimally Invasive Ablative Therapy (MIAT) to prostate in addition to standard of care systemic treatment. The exact treatment protocol and modality used (cryotherapy or high intensity focused ultrasound, HIFU) will be set within the MIAT SOP. For those patients who are undergoing MIAT no local prostate radiotherapy will be given as part of the intervention. Radiotherapy can be given subsequently for palliative reasons.

Intervention Arm 2:
Radical therapy with either prostatectomy or external beam radiotherapy (high radical dose set out in Radiotherapy Intervention Arm 2 SOP) in addition to standard of care systemic treatment. Modality based on physician and patient preference and patient co-morbidities. The surgical technique is at the discretion and expertise of the surgical team but will be laid down in the

Prostatectomy SOP. For those patients who are undergoing radical prostatectomy no local prostate radiotherapy will be given as part of the intervention. Radiotherapy can be given subsequently for palliative reasons.

Metastases Directed Therapy (Intervention Arm 1 and 2):
In both intervention arms 1 and 2, metastases directed therapy (MDT) may be used but intent to use MDT to be declared prior to randomisation. In the case of a metastatic recurrence after MDT, a re-treatment with MDT would be allowed if there were new metastatic areas/locations. The imaging reporting of metastases as well as doses and protocol for MDT will be defined and determined by an Imaging Reporting SOP and a Metastases-Directed Therapy SOP.

In total, 80 men will be approached in 10 UK centre to estimate recruitment rate, acceptability of the trial randomisation, reported toxicities and adherence to trial interventions in a pilot phase. They will also be included into the main phase where 918 will be recruited over 30 UK centres. Participants will remain in the study for a maximum of 4 years. The aims are to see whether men will participate in this trial (pilot) before a larger trial (main) is run, and the impact of these treatments on quality of life.

[68Ga]PSMA-11 PET-CT substudy:
The trialists will also ask men in the pilot part of ATLANTA if they are willing to undergo a PSMA PET scan. They want to see if this scan might be as accurate in detecting residual disease as prostate biopsies and standard body scans, like MRI, CT or bone-scans. This however is optional and participants will be told that they do not have to agree to take part in this optional research, but can still take part in the ATLANTA study. The tests required for this exploratory research will be explained to patients prior to consent in the Patient Information Sheet and verbally by clinician. Target recruitment for this study is 25 patients.

Intervention Type
Mixed

Primary outcome measure
Internal Pilot:
1. Compliance to randomised arm, measured using the electronic Case Report Form on a monthly basis.
2. Recruitment and randomisation rate, measured using the electronic Case Report Form on a monthly basis.
3. Safety (adverse events), measured using the electronic Case Report Form at baseline, week 12, week 26, week 28, week 32, week 34 then every 12 weeks for first year and every 24 weeks for remaining years 2 to 4 for all patients.
4. Proportion of patients with complete pathological response, measured on post SOC systemic therapy prostate biopsies at 6-9 months.

Phase II:
1. Progression-free survival (PFS), with progression defined as a composite outcome of biochemical failure (PSA progression value) or local progression or lymph node progression or bone metastases progression (new sites) or progression or development of new distant metastases, defined as lymph nodes outside the pelvis, bone or organ involvement or skeletal-related events confirmed as progression as in the Systemic Therapy in Advancing Or Metastatic Prostate Cancer: Evaluation Of Drug Efficacy (STAMPEDE) RCT. PFS will be assessed from the time of enrollment to the end of the study. Depending on when the patient is recruited, the follow-up duration will be 2-4 years.

Secondary outcome measures
1. Urinary, sexual and rectal side effects, measured using the IPSS, IIEF15 and EPIC questionnaires at baseline, week 26, week 28, week 34, then every 12 weeks for first year and every 24 weeks for remaining years 2 to 4
2. Patient-reported outcomes, measured using the IPSS, IIEF15, EPIC Bowel and Bladder, EQ-5D-5L, EORTC QLQ-FA12 (Fatigue), EORTC QLQ-ELD14 (Elderly), EORTC QLQ-C30 (General), EORTC QLQ PR25 (Prostate), EORTC QLQ-BM22 (Bone Metastases) questionnaires at baseline, week 26, week 28, week 34, then every 12 weeks for first year and every 24 weeks for remaining years 2 to 4
3. Progression on PSA and imaging and impact of clinical features on progression, measured using PSA blood tests at baseline, week 12, 26, 34 then every 12 weeks for first year and every 24 weeks for remaining years 2 to 4 and Imaging tests at baseline and if progression is suspected by a clinician
4. Health-related quality-of-life, measured using the IPSS, IIEF15, EPIC Bowel and Bladder, EQ-5D-5L, EORTC QLQ-FA12 (Fatigue), EORTC QLQ-ELD14 (Elderly), EORTC QLQ-C30 (General), EORTC QLQ PR25 (Prostate), EORTC QLQ-BM22 (Bone Metastases) questionnaires at baseline, week 26, week 28, week 34, then every 12 weeks for first year and every 24 weeks for remaining years 2 to 4
5. Data on costs and resource utilisation for future cost-effectiveness analysis, measured as defined in the statistical analysis plan at trial completion

Overall study start date
23/02/2017

Completion date
31/08/2026

Eligibility

Key inclusion criteria
1. Diagnosed with prostate cancer within 6 months of screening visit
2. Metastatic disease (Any T, Any N, M1+) of any grade, stage or Prostate Specific Antigen (PSA) level
3. Fit to undergo standard of care treatment for metastatic disease and both minimally invasive therapy and prostate radiotherapy/prostatectomy
4. Performance status 0-2
5. Histologically proven local tumour

Participant type(s)
Patient

Age group
Adult

Sex
Male

Target number of participants
399

Key exclusion criteria
Added 23/08/2023: Current exclusion criteria as of 06/10/2021:
1. Patient did not undergo and/or is unable to undergo standard of care baseline imaging tests for confirmation of metastatic status (CT abdomen/pelvis AND chest X-ray (or CT chest) AND radioisotope bone scan (or whole body imaging such as MRI or PET imaging as alternative to all preceding scans mentioned here) AND prostate MRI.
2. Prior exposure to long-term androgen deprivation therapy or hormonal therapy for the treatment of prostate cancer unless started within 6 months of screening visit.
3. Prior chemotherapy or local or systemic therapy for treatment of prostate cancer (apart from ADT or hormonal therapy as outlined above)

Previous exclusion criteria from 08/02/2021 to 06/10/2021:
1. Patient did not undergo and/or is unable to undergo standard of care baseline imaging tests for confirmation of metastatic status (CT abdomen/pelvis AND chest X-Ray (or CT chest) AND radioisotope bone scan (or whole body imaging such as MRI or PET imaging as alternative to all preceding scans mentioned here) AND prostate MRI
2. Prior exposure to long-term androgen deprivation therapy or hormonal therapy for the treatment of prostate cancer unless started within 4 months of screening visit
3. Prior chemotherapy or local or systemic therapy for treatment of prostate cancer (apart from ADT or hormonal therapy as outlined above in Exclusion Criteria 2)

Previous exclusion criteria:
1. Patient did not undergo and/or is unable to undergo standard of care baseline imaging tests for confirmation of metastatic status (CT abdomen/pelvis AND chest X-Ray (or CT chest) AND radioisotope bone scan (or whole body imaging such as MRI or PET imaging as alternative to all preceding scans mentioned here) AND prostate MRI
2. Prior exposure to long-term androgen deprivation therapy or hormonal therapy for the treatment of prostate cancer unless started within 3 months of randomisation
3. Prior chemotherapy or local or systemic therapy for treatment of prostate cancer (apart from ADT or hormonal therapy as outlined above in Exclusion Criteria 2)

Date of first enrolment
10/04/2019

Date of final enrolment
31/08/2024

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
Charing Cross Hospital, Imperial College Healthcare NHS Trust
Fulham Palace Road, Hammersmith

London
United Kingdom
W6 8RF

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
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SO16 6YD

Study participating centre
Sunderland Royal Hospital
Kayll Road
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United Kingdom
SR4 7TP

Study participating centre
Cambridge Queen Elizabeth Hospital, Kings Lynn
Gayton Road, King's Lynn
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United Kingdom
PE30 4ET

Study participating centre
Northwick Park, London North West Healthcare NHS Trust
Watford Rd
Harrow
United Kingdom
HA1 3UJ

Study participating centre
Freeman Hospital
Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Rd
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Wirral University Teaching Hospital
Wirral University Teaching Hospital NHS Foundation Trust
Arrowe Park Rd
Birkenhead
United Kingdom
CH49 5PE

Study participating centre
Royal Devon and Exeter NHS Trust
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Croydon University Hospital
530 London Road
Thornton Heath
London
United Kingdom
CR7 7YE

Study participating centre
Royal Marsden Hospital
203 Fulham Road
Chelsea
London
United Kingdom
SW3 6JJ

Study participating centre
Glan Clwyd Hospital
North Wales Clinical Research Centre NWCRC
Unit 5 Gwenfro
Wrexham
United Kingdom
LL13 7YP

Study participating centre
Chelsea and Westminister
369 Fulham Road
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United Kingdom
SW10 9NH

Study participating centre
West Middlesex University Hospital
Twickenham Road
Isleworth
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Study participating centre
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United Kingdom
SE5 9RS

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
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Study participating centre
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United Kingdom
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Study participating centre
Wycombe Hospital
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Study participating centre
Oxford University Hospitals NHS Foundation Trust
Churchill Hospital
Old Road
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Oxford
United Kingdom
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Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
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Study participating centre
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Sponsor information

Organisation
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Sponsor details
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Sponsor type
University/education

Website
https://www.imperial.ac.uk/joint-research-compliance-office/

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Research organisation

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Main study:
When the study is completed the results will be analysed and presented at international meetings before being published in a medical journal. Large studies such as this take many years to complete and for the final results to appear. When the study results are concluded, they will be presented by clinicians and patient groups, and posted on our website for patients to access. The trial website is available via a link on this page. A newsletter presenting the salient findings in an easy-to-read style will be written in conjunction with the patient representative at study end. This will be circulated to all consenting participants by email or letter depending on their preferences. Findings will be presented through the websites and newsletter of a number of supporting organisations of which our team members have links including Prostate Cancer UK, Maggie’s support group, Pelican Cancer Foundation and CRUK. The social media presence of organisations involved will be used to highlight news about the trial.

Sub-study results:
After completion of the study the results may be presented at national/international scientific meetings or published in a leading medical journal. The patient will not be identified in any report/publication, and the patient is made aware that the results of some of the tests done as a part of this research may not be available to them individually. Data and images obtained from the scans may be used in an anonymous form for future research, including that carried out by commercial healthcare companies. The participants will not be contacted by any companies carrying out such research and they will not be given access to the participants medical records. It is also made clear in the sub-study PIS that if any inventions resulting in commercial gain emerge from any of this research the participant will not be eligible to benefit financially from these discoveries.

Intention to publish date
31/01/2027

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Hashim U Ahmed (hashim.ahmed@imperial.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No