ISRCTN74358648 https://doi.org/10.1186/ISRCTN74358648

Add-Aspirin: the effects of aspirin on disease recurrence and survival after primary therapy in common non-metastatic solid tumours.

Submission date 21/01/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 21/01/2015	**Overall study status** Ongoing	
Last Edited 06/06/2025	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-whether-aspirin-can-stop-cancer-coming-back-after-treatment-add-aspirin

Study website
http://www.addaspirintrial.org/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2013-004398-28

IRAS number

120104

ClinicalTrials.gov number
NCT02804815

Secondary identifying numbers
18067, IRAS 120104

Study information

Scientific Title
A phase III double-blind placebo-controlled randomised trial assessing the effects of aspirin on disease recurrence and survival after primary therapy in common non-metastatic solid tumours.

Study objectives
Aim: To assess whether regular aspirin use after standard cancer therapy prevents recurrence and prolongs survival in patients with early stage common solid tumours. International recruitment will allow assessment of the intervention in different communities.

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/SC/0171; First MREC approval date 04/06/2014

Study design
Randomized; Interventional

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 patient information sheet

Health condition(s) or problem(s) studied
Cancer

Interventions
1. Randomised blinded phase: Participants will be randomly assigned to 100 mg aspirin, 300 mg aspirin or matched placebo. All tablets will be enteric-coated to be taken daily for at least five years

2. Run-in feasibility phase: During the feasibility phase of the study, all participants will take open label 100 mg aspirin daily for a run-in period of approximately 8 weeks prior to randomisation

Intervention Type
Other

Phase
Phase III

Primary outcome measure
Overall survival

Secondary outcome measures
Added 07/12/2023:
1. Adherence, toxicity including serious haemorrhage, and cardiovascular events, recorded on the study-specific CRFs at each visit. Participants are asked how often they took their tablets at every visit and if they have experienced new or worsening symptoms; the CRF also lists aspirin-related toxicities which are asked about and graded by the clinician.
2. Tumour-specific items such as scan (eg. CT) and tests (e.g. prostate-specific antigen (PSA) are recorded at each study visit once study treatment has started

Overall study start date
01/03/2015

Completion date
31/10/2026

Eligibility

Key inclusion criteria
Common inclusion criteria:
1. Written informed consent
2. WHO performance status 0, 1 or 2
3. Previous or current participants of other primary treatment trials if agreed in advance between trials
4. No clinical or radiological evidence of residual or distant disease

Breast cohort inclusion criteria:
1. Men or women with histologically confirmed invasive breast cancer
2. Undergone complete primary invasive tumour excision with clear margins
3. Surgical staging of the axilla must have been undertaken by sentinel node biopsy, axillary sampling or dissection
4. In those patients with a positive sentinel node biopsy:
4.1. If 1, 2 or 3 nodes are positive, subsequent management of the axilla (with surgery, radiotherapy or no further intervention) should be completed prior to registration
4.2. If 4 or more nodes are involved, patients must have undergone completion axillary node dissection
5. Radiotherapy (RT):
5.1. Patients who have undergone breast-conserving surgery should receive adjuvant RT
5.2. Patients who have undergone mastectomy should receive RT if they have more than 3

axillary lymph nodes involved
5.3. Patients who have undergone mastectomy and have T3 tumours and/or 1, 2 or 3 involved lymph nodes may (or not) receive radiation per institutional practice
6. Final histology must fall within at least one of these 3 groups:
6.1. Node positive
6.2. Node negative with high-risk features 2 or more of:
6.2.1. ER negative
6.2.2. HER2 positive
6.2.3. Grade 3
6.2.4. Lymphovascular invasion present
6.2.5. Age <35
6.2.6. Oncotype Dx score of >25
6.3. In patients who have received neoadjuvant chemotherapy, patients are eligible if they have both a hormone receptor negative/HER2 negative tumour, a HER2 positive tumour or a hormone receptor positive grade 3 tumour and did not achieve a pathological complete response with neoadjuvant systemic therapy
7. Patients who received standard neoadjuvant and/or adjuvant chemotherapy or RT are eligible
8. Known HER2 and ER status
9. Participants may receive endocrine therapy and trastuzumab. All ER-positive patients should be planned to undergo at least 5 years of adjuvant endocrine therapy

Colorectal cohort inclusion criteria:
1. Histologically confirmed stage II or III adenocarcinoma of the colon or rectum and patients who have undergone resection of liver metastases with clear margins and no residual metastatic disease
2. Patients with synchronous tumours if one of the tumours is at least stage II or III
3. Serum CEA ideally =1.5 x upper limit of normal
4. Have undergone curative (R0) resection with clear margins

Gastroesophageal cohort inclusion criteria:
1. Patients with histologically confirmed adenocarcinoma, adenosquamous carcinoma or squamous cell cancer of the oesophagus, gastroesophageal junction or stomach
2. Have undergone curative (R0) resection with clear margins or primary chemoRT given with curative intent

Prostate cohort inclusion criteria:
1. Men with histologically confirmed node negative nonmetastatic
adenocarcinoma of the prostate
2. Have undergone curative treatment, either:
2.1. Radical prostatectomy
2.2. Radical RT
2.3. Salvage RT (following rise in PSA after prostatectomy)
3. Intermediate or high risk according to D'Amico classification

Treatment pathway-specific inclusion criteria:
1. Prostatectomy patients:
1.2. Open, laparoscopic or robotic radical prostatectomy
1.3. Men treated with immediate adjuvant RT
1.4. Men receiving adjuvant hormone therapy planned for a maximum duration of 3 years
1.5. Men randomised to any of the 3 arms of RADICALS HD are eligible Prostatectomy patients
2. Radical RT patients:
2.1. Men receiving neoadjuvant and/or adjuvant hormone therapy planned for a maximum

duration of 3 years
3. Salvage RT patients following PSA rise after previous radical prostatectomy:
3.1. Men treated with salvage RT following a rise in PSA are eligible
3.2. Men receiving neo and/or adjuvant hormone therapy planned for a maximum of 3 years
3.3. Men randomised to any of the 3 arms of RADICALS HD are eligible

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 11000; UK Sample Size: 9189

Total final enrolment
10268

Key exclusion criteria
Participants must not meet any of the common or their tumour specific exclusion criteria.

Common exclusion criteria:
1. Current or previous regular use of aspirin (at any dose) or current use of another NSAID for any indication
2. A past history of adverse reaction or hypersensitivity to NSAIDs, celecoxib, aspirin or other salicylates or sulphonamides, including asthma, that is exacerbated by use of NSAIDs
3. Current use of anticoagulants
4. Current or longterm use of oral corticosteroids. The treating physician should make the clinical decision whether a patient has been exposed to longterm therapy
5. Active or previous peptic ulceration or gastrointestinal bleeding within the last year, except where the cause of bleeding has been surgically removed
7. Active or previous history of inflammatory bowel disease
8. History of moderate or severe renal impairment, with eGFR<45ml/min/1.73m2.
9. Previous invasive or noninvasive malignancy except:
9.1. DCIS where treatment consisted of resection alone.
9.2. Prostate cancer initially treated with prostatectomy and now being treated with salvage radiotherapy following a rise in PSA.
9.3. Cervical carcinoma in situ where treatment consisted of resection alone.
9.4. Basal cell carcinoma where treatment consisted of resection alone or radiotherapy.
9.5. Superficial bladder carcinoma where treatment consisted of resection alone.
9.6. Other cancers where the patient has been disease free for =15 years.
10. Any other physical condition which is associated with increased risk of aspirin related morbidity or, in the opinion of the Investigator, makes the patient unsuitable for the trial, including but not limited to severe asthma, haemophilia and other bleeding diatheses, macular degeneration and patients with a high risk of mortality from another cause within the trial

treatment period
11. Known glucose6phosphate dehydrogenase deficiency
12. Known lactose intolerance
13. LFTs greater than 1.5x the upper limit of normal unless agreed with TMG
14. Anticipated difficulties in complying with trial treatment or followup schedules
15. <16 years old
16. Participants in other treatment trials where this has not been agreed in advance by both trial teams
17. Pregnant or breast feeding, or intending to become pregnant or breast feed during the trial treatment period

Breast cohort exclusion criteria:
1. Metastatic or bilateral breast cancer.

Colorectal cohort exclusion criteria:
1. Proven (or clinically suspected) metastatic disease (patients who have undergone resection of liver metastases with clear margins and no residual metastatic disease are eligible)

Gastroesophageal cohort exclusion criteria:
1. Proven (or clinically suspected) metastatic disease.

Prostrate cohort participant criteria:
1. Biopsy proven or radiologically suspected nodal involvement, or distant metastases from prostate cancer
2. Adjuvant hormone therapy planned for >3 years
3. Bilateral orchidectomy

Date of first enrolment
01/03/2015

Date of final enrolment
01/01/2025

Locations

Countries of recruitment
England

India

Ireland

United Kingdom

Study participating centre
Medical Research Council Clinical Trials Unit (MRC CTU)
90 High Holborn
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London

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Sponsor information

Organisation
University College London

Sponsor details
Gower Street
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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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
Results from each of the four tumour-specific cohorts will be submitted (separately) for publication in high impact peer-reviewed journals; timelines differ for the different cohorts with expected dates for dissemination between June 2026 and December 2027.

Intention to publish date
31/12/2027

Individual participant data (IPD) sharing plan
Access to data or samples will be via application to the Trial Steering Committee (TSC) and will be managed according to the standard policy and process in place at the MRC Clinical Trials Unit at UCL. Applicants will need to provide details of the data/samples being requested, the proposed study, funding and ethical approvals, and the credentials of the research group. Participants provide consent for future use of data and samples in ethically approved research studies.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	feasibility analysis	01/11/2019	02/06/2020	Yes	No
Abstract results		26/05/2019	14/11/2022	No	No
HRA research summary			28/06/2023	No	No