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6-mercaptopurine (6MP) and low-dose methotrexate in patients with known BRCA defective tumours

Submission date 06/05/2011	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/05/2011	**Overall study status** Completed	
Last Edited 23/03/2023	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-mercaptopurine-and-methotrexate-for-advanced-breast-or-ovarian-cancer-people-with-brca-gene-faults

Study website
http://www.oncology.ox.ac.uk/trial/6mp

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2009-016846-16

IRAS number

ClinicalTrials.gov number
NCT01432145

Secondary identifying numbers
9671

Study information

Scientific Title
Phase II clinical trial of 6-mercaptopurine (6MP) and low-dose methotrexate in patients with known BRCA defective tumours

Study objectives
This study will evaluate the efficacy and safety of 6MP in combination with methotrexate in patients with breast or ovarian cancer who are known to have a BRCA mutation. 6MP is used instead of 6- Thioguanine (6TG) as it is converted to the same cytotoxic moiety as 6TG, ie. thioguanine nucleotides, but with reduced toxic effects. Low dose methotrexate is used in combination with 6MP as it promotes the formation of thioguanine nucleotides.

On 06/11/2014 the anticipated end date was changed from 30/09/2015 to 31/12/2014.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire REC B, first MREC approval date 24/01/2011, ref: 10/H0605/79

Study design
Non-randomised; Interventional; Design type: Screening, Treatment

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied

Topic: National Cancer Research Network; Subtopic: Breast Cancer, Gynaecological Cancer; Disease: Breast, Ovary

Interventions
Mercaptopurine, The dose of 6MP will be 75mg/m2 body surface area, administered orally (PO) once a day (od) in the morning 1 hour after eating, on a continuous schedule. Tablets should be taken at roughly the same time each day; methotrexate (20 mg/m2) will be taken orally, once a week, in the morning.; Follow Up Length: 24 month(s); Study Entry : Registration only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
6-mercaptopurine, methotrexate

Primary outcome measure
Objective tumour response rate (radiological) at 8 weeks.; Timepoint(s): 8 weeks

Secondary outcome measures
1. Assessment of feasibility as a multi-centre study; Timepoint(s): End of study
2. Assessment of quality of life.; Timepoint(s): Baseline,3 months, 6 months, end of treatment or 12 months
3. Assessment of the safety and toxicity of 6MP and low dose methotrexate; Timepoint(s): Duration of study
4. Biochemical response rates (ovarian cancer patients only); Timepoint(s): Duration of the study
5. Overall survival at 1 and 2 years post entry into the study; Timepoint(s): Up to 2 years post study entry
6. Progression free survival.; Timepoint(s): Duration of study

Overall study start date
01/04/2011

Completion date
31/12/2014

Eligibility

Key inclusion criteria
Patients with proven BRCA1 or BRCA2 mutations and after appropriate exposure to standard treatment, as defined by:
1. Breast cancer
1.1. Patients with initially histologically or cytologically proven locally advanced or metastatic breast cancer who may have received up to 3 previous lines of chemotherapy in the locally advanced or metastatic breast cancer setting
1.2. Patients must have previously had a taxane and an anthracycline in either the adjuvant or metastatic setting, provided that these were not contraindicated

1.3. Patients with hormone responsive disease should have had at least one line of hormone therapy for metastatic disease
1.4. Prior treatment with a Poly (ADP-ribose) polymerase (PARP) inhibitor is permissible
2. Ovarian cancer
2.1. Patients with initially histologically or cytologically proven ovarian cancer
2.2. Patients must have disease that is platinum resistant or in whom further platinum based therapy is inappropriate
2.3. Prior treatment with a PARP inhibitor is permissible
3. Patients must have measurable disease on computerised tomography (CT) or magnetic resonance imaging (MRI) scan as defined by Response Evaluation Criteria In Solid Tumors (RECIST) criteria
4. Age more than or equal to 18 years
5. ECOG performance score of 0-2
6. Life expectancy of > 12 weeks
7. Adequate haematological and biochemical function
8. Written informed consent; Target Gender: Female ; Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 65; UK Sample Size: 65; Description: 65 patients with confirmed BRAC1 or BRAC2 mutant status

Total final enrolment
67

Key exclusion criteria
1. Patients with any of the following contra-indications to thiopurines (6MP/6TG) or methotrexate:
1.1. Family history of severe liver failure
1.2. Porphyria
1.3. Diffuse infiltrative pulmonary or pericardial disease
1.4. Known hypersensitivity to either trial agent
2. Patients found to have a Low/Low genotype on Thiopurine S-methyl transferase (TPMT) testing
3. Pregnant or breast-feeding women
4. Other active malignancy, with the exception of adequately treated in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin
5. Patients known or tested to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus (HIV)
6. Patients with active CNS lesions are excluded (i.e., those with radiographically unstable,

symptomatic lesions). However, patients treated with stereotactic therapy or surgery and/or whole brain radiotherapy are eligible if the patient remains without evidence of disease progression in brain = 3 months prior to registration date . They must also be off corticosteroid therapy for = 3 weeks prior to registration date.
7. Patients who have received anticancer agent(s) or an investigational agent within 28 days prior to study drug administration
8. Subjects who have not recovered to within one grade level (not to exceed grade 2) of their baseline following a significant adverse event or toxicity attributed to previous anticancer treatment

Date of first enrolment
01/04/2011

Date of final enrolment
20/10/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Clinical Oncology
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Sponsor information

Organisation
University of Oxford (UK)

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Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) - Clinical Trials Advisory and Awards Committee (CTAAC)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

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	19/12/2014	10/04/2019	Yes	No
Basic results			20/05/2019	No	No
Plain English results			23/03/2023	No	Yes
HRA research summary			28/06/2023	No	No