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Phase 1 trial of olaparib with temozolomide in relapsed glioblastoma

Submission date 10/08/2011	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 10/08/2011	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 25/04/2019	**Condition category** Cancer	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-olaparib-with-temozolomide-glioblastoma-has-come-back

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-018615-15

IRAS number

ClinicalTrials.gov number
NCT01390571

Secondary identifying numbers
10482

Study information

Scientific Title
A Cancer Research UK Phase I trial of olaparib (AZD2281), an oral PARP Inhibitor, in combination with extended lowdose oral temozolomide in patients with relapsed glioblastoma

Acronym
OPARATIC

Study objectives
This is the first combination study of olaparib with temozolomide and with olaparib in patients with glioblastoma. Stage 1 requires six patients to be treated with olaparib prior to recurrent resection surgery. Evidence of olaparib in tumour biopsy material combined with evidence of PARP inhibition and DCE and DW MRI will explore the permeability of the blood brain barrier to olaparib in patients with recurrent glioblastoma. Stage 2 involves a dose escalation of combination treatment with extended low dose temozolomide and olaparib to find the MTD in the same recurrent patient population post-resection. Ten further patients will then be treated at the combination MTD and will undergo funcional MRI.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First MREC, 28/04/2011, ref: 11/AL/0213

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

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Brain Tumour

Interventions

1. DCE/DW MRI, Dual baseline and one post-administration DCE/DW MRI scans to observe the permeability of the blood brain barrier.
2. Administration of olaparib PARP inhibitor prior to surgery followed by combination treatment with low dose temozolomide in 42 day cycles

Intervention Type
Other

Phase
Phase I

Primary outcome measure
1. Identification of combination MTD
2. Reporting of safety information at every patient visit and throughout the trial

Secondary outcome measures
1. Demonstration of olaparib in tumour tissue
2. Resection

Overall study start date
18/07/2011

Completion date
02/01/2017

Eligibility

Key inclusion criteria
1. Histological proven glioblastoma (World Health Organisation[WHO] Grade 4).
2. Radiological diagnosis of recurrent or progressive disease according to RANO criteria, which is suitable for palliative resection.
3. Patients should have enough resectable tumour tissue for sampling requirements in the opinion of the neurosurgeon.
4. Prior 1st line treatment with radical radiotherapy, or chemoradiation followed by adjuvant chemotherapy (no prior
chemotherapy for recurrent disease is allowed).
5. Aged between 18 and 70 years.
6. Life expectancy > 12 weeks
7. WHO performance status of 02
8. Haematological and biochemical indices within the ranges shown below. These measurements must be performed within one week before the patient goes on study.
Haemoglobin (Hb) = 9.0 g/dL
Absolute neutrophil count (ANC) = 1.5 x 109/L
Platelet count = 100 x 109/L
Serum bilirubin = 1.5 x upper limit of normal (ULN)
ALT or AST = 2.5 x ULN
Either: Calculated creatinine clearance = 50 mL/min Or: Isotope clearance measurement = 50 mL /min (uncorrected)

9. Ability to swallow and retain oral medications.
10. Written (signed and dated) informed consent and be capable of cooperatingwith treatment, scans and followup

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
Planned Sample Size: 28; UK Sample Size: 28

Total final enrolment
45

Key exclusion criteria
1. Radiotherapy, endocrine therapy or immunotherapy during the previous 12 weeks before treatment, or chemotherapy during the 4 weeks before treatment.
2. Any previous treatment with a PARP inhibitor, including olaparib.
3. Ongoing toxic manifestations of previous treatments. Exceptions to this are alopecia or Grade 1 toxicities, which in the opinion of the Investigator and the Drug Development Office (DDO) should not exclude the patient.
4. Change to systemic steroids dose within the five days prior to enrolment (ie. must be on a stable dose at time of
enrolment).
5. Ability to become pregnant (or already pregnant or lactating). However, those female patients who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have a intrauterine
device and condom, diaphragm with spermicidal gel and condom) for four weeks before entering the trial, during the trial and for six months afterwards are
considered eligible.
6. Male patients with partners of childbearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] during the trial and for six months afterwards). Men with pregnant or lactating partners should be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure to the foetus or neonate.
7. Major thoracic or abdominal surgery from which the patient has not yet recovered.
8. At high medical risk because of nonmalignant systemic disease including active uncontrolled infection.
9. Known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency

virus (HIV).
10. Concurrent congestive heart failure, prior history of class III/ IV cardiac disease (New York Heart Association [NYHA]
refer to Appendix 3), prior history of cardiac ischaemia or prior history of cardiac arrhythmia within the previous 12 months.
11. Patients with pacemakers, a history of previous heart surgery, any major surgery in the preceding six weeks, metal fragments in their eyes, shrapnel or bullet injuries are excluded (on the basis of their unsuitability to undergo MRI scans). Patients with metal implants or tattoos should be discussed with MRI staff.
12. Grand mal seizures occurring = 3 times per week over the past month.
13. Patients with gastrointestinal disorders likely to interfere with absorption of the study medication.
14. Patients taking drugs known to be potent inhibitors or inducers of CYP3A4 including phenytoin, carbamazepine and phenobarbitone which cannot be stopped for the duration of the trial.
15. Immunisations with live vaccines received within the previous four weeks (or expected to receive during the trial and up to at least six months after receiving last study treatment). Including BCG and yellow fever.
16. Known hypersensitivity to any of the components of olaparib.
17. Known hypersensitivity to temozolomide (TMZ), or to any of its components, or to dacarbazine (DTIC) (Stage 2 only).
18. Known lactose intolerance (Stage 2 only)
19. Is a participant or plans to participate in another interventional clinical study, whilst taking part in this Phase I study. Participation in an observational study would be acceptable.
20. Any other condition which in the Investigators opinion would not make the patient a good candidate for the clinical trial.

Date of first enrolment
18/07/2011

Date of final enrolment
02/01/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Drug Development Office, Angel Building , 407 St. John Street
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Sponsor information

Organisation
Cancer Research UK

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Drug Development Office, PO Box 123
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Sponsor type
Charity

ROR
https://ror.org/054225q67

Funder(s)

Funder type
Charity

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
Not provided at time of registration

Intention to publish date

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?
Plain English results				No	Yes
HRA research summary			28/06/2023	No	No