

# Phase 1 trial of olaparib with temozolomide in relapsed glioblastoma

<b>Submission date</b> 10/08/2011	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 10/08/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 25/04/2019	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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

### Contact name

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### Contact details

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## Additional identifiers

### ClinicalTrials.gov (NCT)

NCT01390571

### Clinical Trials Information System (CTIS)

2010-018615-15

### Protocol serial number

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 functional 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

## Study type(s)

Treatment

## 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(s)

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

**Key secondary outcome(s)**

1. Demonstration of olaparib in tumour tissue
2. Resection

**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) =  $1.5 \times 10^9/L$   
Platelet count =  $100 \times 10^9/L$   
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 cooperating with treatment, scans and followup

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

70 years

## Sex

All

## 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**

United Kingdom

England

**Study participating centre**

**Drug Development Office, Angel Building , 407 St. John Street**

London

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EC1V 4AD

## **Sponsor information**

**Organisation**

Cancer Research UK

**ROR**

<https://ror.org/054225q67>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

Cancer Research UK

**Alternative Name(s)**

CR\_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

#### IPD sharing plan summary

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>				No	Yes