

# Olaparib and radiotherapy in newly-diagnosed glioblastoma

<b>Submission date</b>	<b>Recruitment status</b>	<input checked="" type="checkbox"/> Prospectively registered
02/05/2014	No longer recruiting	<input type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
02/06/2014	Completed	<input type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
16/12/2025	Cancer	<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-olaparib-and-radiotherapy-for-people-with-glioblastoma-paradigm>

## Contact information

### Type(s)

Scientific

### Contact name

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### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2014-001216-19

### Protocol serial number

GN13ON355

# Study information

## Scientific Title

Short-course radiotherapy plus olaparib for newly diagnosed glioblastoma in patients unsuitable for radical chemoradiation: a randomised phase II clinical trial preceded by a lead-in phase I dose escalation study

## Acronym

PARADIGM

## Study objectives

The objective of phase I is to establish the maximum tolerated dose of olaparib when given in combination with radiotherapy.

The objectives of phase II are to obtain evidence that adding olaparib to radiotherapy improves overall survival in this patient population, and to justify a subsequent phase III trial.

Additional objectives are to document the safety, toxicity and quality of life associated with this combination.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 13/11/2014, West of Scotland Research Ethics Service (West of Scotland REC 1, Admin Building, Level 2, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, G12 0XH, UK; ggc.wosrec1@nhs.scot), ref: 14/WS/1096

## Study design

Phase I dose-escalation study followed by a Phase II randomized double-blind study

## Primary study design

Interventional

## Study type(s)

Treatment

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

Gliomas

## Interventions

All patients will receive hypofractionated, short-course radiotherapy (40 Gray in 15 fractions) over 19 °C 21 days. In the Phase I component, escalating doses of oral olaparib will be delivered daily throughout the radiotherapy treatment period. Olaparib will be commenced 3 days prior to radiation and will continue throughout treatment for a total of 22 - 24 days.

In Phase II, patients will be randomised to receive radiotherapy plus placebo PO (control arm) or radiotherapy plus olaparib PO at the maximum tolerated dose (MTD) established in Phase I (or a maximum dose of 200 mg PO twice daily if MTD not reached). Olaparib or placebo will be commenced 3 days prior to radiation and will continue throughout treatment for a total of 22 - 24 days.

**Intervention Type**

Drug

**Phase**

Phase I/II

**Drug/device/biological/vaccine name(s)**

Olaparib

**Primary outcome(s)**

Phase I: The recommended dose of olaparib when administered in combination with radiotherapy

Phase II: Overall survival

**Key secondary outcome(s)**

Phase I: The DLT (Dose-Limiting Toxicity) and the safety and tolerability of olaparib administered in combination with radiotherapy.

Phase II:

1. Progression-free survival measured by MRI scans during follow-up and will be assessed in accordance with the RANO guidelines
2. Toxicity measured using the CTCAE v4.0 criteria and recorded at each follow-up visit
3. Quality of life which will be measured by the completion of QLQ30, BN20 and EQ-5D questionnaires completed by the participant at baseline and each follow-up visit

**Completion date**

31/12/2025

## Eligibility

**Key inclusion criteria**

1. Age 18 - 69 years: WHO performance status 2 at initial oncology consultation or performance status 0-1 but otherwise unsuitable for radical radiotherapy with concomitant and adjuvant temozolomide.
2. Age over 70 years: WHO performance status 0 or 1 at initial oncology consultation
3. Histologically confirmed diagnosis of glioblastoma
4. Life expectancy greater than 12 weeks
5. No previous radiotherapy or chemotherapy for primary or secondary CNS malignancy
6. Adequate haematological, hepatic and renal function defined as below:  
Haemoglobin  $\geq$  9.0 g/dL, absolute neutrophil count  $\geq$  1.5 x 10<sup>9</sup>/L, platelet count  $\geq$  100 x 10<sup>9</sup>/L, bilirubin  $\leq$  1.5 x upper limit of normal (ULN), Alanine aminotransferase (ALT) or aspartate aminotransferase (AST)  $\leq$  2.5 x ULN, Adequate renal function with creatinine clearance / glomerular filtration rate  $>$  50 ml/min. If the creatinine clearance / glomerular filtration rate is less than 50 ml/min as calculated by the Cockroft-Gault/Wright formula, then the creatinine clearance / glomerular filtration rate should be measured by either a radio-isotope technique or by 24-hour urine collection.
7. Ability to provide written informed consent prior to participating in the trial and any trial related procedures being performed

8. Willingness to comply with scheduled visits, treatment plans and laboratory tests and other trial procedures
9. Ability to swallow oral tablets/capsules

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

18 years

**Upper age limit**

100 years

**Sex**

All

**Total final enrolment**

172

**Key exclusion criteria**

1. WHO performance status >2
2. Life expectancy less than 12 weeks
3. Active concurrent malignancy (except non-melanoma skin cancer or in situ carcinoma of the cervix). If history of prior malignancy, must be disease-free for >5 years.
4. Prior treatment for primary or secondary CNS malignancy
5. Confusion or altered mental state that would prohibit understanding and giving of informed consent
6. Concomitant treatment with medicines detailed in section 5.10 of protocol.
7. Female patients who are able 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 an intra-uterine device and condom, diaphragm with spermicidal gel and condom) effective at the first administration of either IMP, throughout the trial, and for six months afterwards, are considered eligible.
8. Male patients with partners of child-bearing potential (unless they agree to take measures not to father children by using one form of highly effective contraception [condom plus spermicide] effective at the first administration of IMP, throughout 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.
9. Administration of any investigational drug within 28 days of receiving the first dose of trial treatment.

**Date of first enrolment**

03/03/2015

**Date of final enrolment**

31/03/2025

## Locations

**Countries of recruitment**

United Kingdom

Scotland

**Study participating centre**

**Beatson West of Scotland Cancer Centre**

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## Sponsor information

**Organisation**

NHS Greater Glasgow and Clyde (UK)

**ROR**

<https://ror.org/05kdz4d87>

## Funder(s)

**Funder type**

Industry

**Funder Name**

Astra Zeneca (UK) - endorsed by Cancer Research UK

## Results and Publications

**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Data sharing statement to be made available at a later date

## 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="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes