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Olaparib and radiotherapy In newly-diagnosed glioblastoma

Submission date 02/05/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/06/2014	**Overall study status** Ongoing	
Last Edited 14/02/2025	**Condition category** Cancer	

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

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Additional identifiers

EudraCT/CTIS number
2014-001216-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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)
West of Scotland Research Ethics Service, 13/11/2014, ref: 14/WS/1096

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

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 the contact details to request a patient information sheet

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 measure
Phase I: The recommended dose of olaparib when administered in combination with radiotherapy
Phase II: Overall survival

Secondary outcome measures
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 v.4.0 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

Overall study start date
01/11/2014

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Age 18 - 69: 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: 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 >/= 9.0 g/dL, absolute neutrophil count >/= 1.5 x 109/L, platelet count >/= 100 x 109/L, bilirubin </= 1.5 x upper limit of normal (ULN), Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) </= 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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Phase I 12-24 patients. Phase II - 140 patients.

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
Scotland

United Kingdom

Study participating centre
The Beatson West of Scotland Cancer Centre
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Sponsor information

Organisation
NHS Greater Glasgow and Clyde (UK)

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Sponsor type
Hospital/treatment centre

Website

http://www.nhsggc.org.uk/r&d

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Industry

Funder Name
Astra Zeneca (UK) - endorsed by Cancer Research UK

Results and Publications

Publication and dissemination plan
Planned publication in high impact medical journals and presentation at national meetings.

Intention to publish date
01/04/2026

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?
HRA research summary			28/06/2023	No	No