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Trial of ipilimumab immunotherapy in recently diagnosed glioblastoma brain tumours

Submission date 12/11/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 12/11/2018	**Overall study status** Completed	
Last Edited 27/05/2025	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-ipilimumab-and-temozolomide-for-people-with-glioblastoma-ipi-glio

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-000095-15

Integrated Research Application System (IRAS)
238638

Protocol serial number
CPMS 37562, IRAS 238638

Study information

Scientific Title
A Phase II, open label, randomised study of ipilimumab with temozolomide versus temozolomide alone after surgery and chemoradiotherapy in patients with recently diagnosed glioblastoma (IPI-GLIO)

Acronym
IPI-GLIO

Study objectives
Glioblastoma is the most common malignant primary brain tumour. The trialists are trying to find out whether after chemoradiotherapy it is better to continue with standard treatment with temozolomide, or if adding a drug called ipilimumab to standard treatment is better in terms of survival and/or safety and tolerability. They hypothesise that adding ipilimumab to standard treatment is better.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central – Oxford B Research Ethics Committee, 02/11/2018, ref: 18/SC/0525

Study design
Randomized; Interventional; Design type: Treatment, Drug, Immunotherapy

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current interventions as of 07/06/2021:
This is an unblinded, open labelled stratified randomised Phase II multicentre clinical trial (CTIMP). Patients with newly diagnosed de-novo glioblastoma following surgery and radical radiotherapy with concomitant temozolomide will be recruited from hospitals in the UK.

The study will have statistical power of 80% to show a significant difference between 22.5-month median survival in the ipilimumab and temozolomide arm and 15-month median survival in the temozolomide arm. To allow this, 120 patients need to be recruited (80 to the ipilimumab and temozolomide arm and 40 to the temozolomide arm) This assumes an 18 month recruitment period and survival follow-up for a minimum of 18 months after the last participant randomised (maximum of 5 years after individual participant randomisation) and 72 events. A 2:1 randomisation was chosen to aid recruitment and because there is already 10 years of experience of temozolomide in the public domain.

All analyses will be on an intention-to-treat basis. This means that patients will be analysed as they are randomised irrespective of the treatment actually received. The intention-to-treat population will include all patients who have given their informed consent and for whom there is confirmation of successful allocation of a randomisation number. It is therefore important that every effort is made to encourage patients, including those patients who do not receive /complete their allocated treatment, to attend for follow-up clinic visits to avoid bias in the analysis of the results. No interim analyses are planned.

Patients will be randomly allocated in a 2:1 ratio to receive either:
Arm A: ipilimumab + temozolomide, 80 patients
Arm B: temozolomide, 40 patients

Ipilimumab given by intravenous infusion at a dosage of 3mg/kg every 3 weeks for a total of 4 doses.

Temozolomide is taken orally for 6 cycles. Each cycle is 28 days long once daily for 5 days followed by 23 days without treatment. Patients take 150 mg/m^2/day for Cycle 1 (Dose Level 0), and then 200 mg/m^2/day (Dose Level 1) during Cycles 2-6 in the absence of toxicity except

in cases as described in the protocol where it is taken at Dose Level -1. The dose may be reduced to 100 mg/m^2/day (Dose Level -1) in case of toxicity.

The duration of study treatment is 24 weeks and the end of study visit is at 52 weeks. Survival data and other information relevant to survival will be collected from medical records at 2 and 3 years from individual participant randomisation dates and at a timepoint up to 18 months from 30th April 2021, which is anticipated to be near the date the last patient is randomised. No 2- and /or 3-year follow-up will occur after 18 months from 30th April 2021. Progression-free survival will be collected at 18 months from 30th April 2021.

Previous interventions:
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The study will have statistical power of 80% to show a significant difference between 22.5-month median survival in the ipilimumab and temozolomide arm and 15-month median survival in the temozolomide arm. To allow this, 120 patients need to be recruited (80 to the ipilimumab and temozolomide arm and 40 to the temozolomide arm) This assumes an 18 month recruitment period and survival follow-up for a minimum of 18 months after the last participant randomised (maximum of 5 years after individual participant randomisation). A 2:1 randomisation was chosen to aid recruitment and because there is already 10 years of experience of temozolomide in the public domain.

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The duration of study treatment is 24 weeks and the end of study visit is at 52 weeks. Survival data and other information relevant to survival will be collected from medical records at 18 months from the last participant's randomisation and 2, 3, and 5 years from individual participant randomisation dates.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Ipilimumab, temozolomide

Primary outcome(s)
Overall survival (OS). The treatment comparison will be reported as the hazard ratio (HR) plus 80% confidence interval. 18-month survival rates per treatment groups will be reported; Timepoint(s): 18 months from the last patient's randomisation

Key secondary outcome(s))
Current secondary outcome measures as of 07/06/2021:
1. Any toxicity grade ≥3 graded according to CTCAE v4.03 and length of time for toxicity to resolve; Timepoint(s): From the time of patient consent until patient's end of study
2. Overall survival at 3 years including a treatment effect reported as a hazard ratio; Timepoint (s): 3 years from the patient's randomisation date
4. Progression-free survival (PFS) measured at 18 months from 30th April 2021

Previous secondary outcome measures:
1. Any toxicity grade ≥3 graded according to CTCAE v4.03 and length of time for toxicity to resolve; Timepoint(s): From the time of patient consent until patient's end of study
2. Overall survival at 5 years including a treatment effect reported as a hazard ratio; Timepoint (s): 5 years from the patient's randomisation date

Completion date
31/10/2022

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 24/04/2023:
1. Newly diagnosed histologically-confirmed de-novo supratentorial glioblastoma (including gliosarcoma), by WHO guidelines with >20% surgical debulking (surgeon defined)
2. Radiotherapy to have begun within 49 days of surgery
3. Completed standard radiotherapy and concurrent temozolomide
4. Clinically appropriate for adjuvant temozolomide and capable of completing adjuvant temozolomide without dose reduction, based on investigator judgement
5. Male or female, age 18-70 years
6. Life expectancy of at least 12 weeks
7. ECOG performance status of 0-1
8. The patient is willing and able to comply with the protocol scheduled follow-up visits and examinations for the duration of the study
9. Written (signed and dated) informed consent
10. Haematological and biochemical indices within stated ranges
Lab Test Value required:
Haemoglobin (Hb) ≥9 g/dL (blood transfusions not permitted to maintain haemoglobin)
Platelet count ≥100 x 109/L
Absolute Neutrophil Count ≥1.0 x 109/L (G-CSF not permitted to maintain ANC)
Lymphocyte count ≥0.5 x 109/L

Serum creatinine < 1.5 x ULN or a creatinine clearance of ≥ 50mL/min calculated by Cockcroft-Gault formula
Female CrCl = (140-age in years) x weight in kg x 1.04 serum creatinine in µmol/L
Male CrCl = (140-age in years) x weight in kg x 1.23 serum creatinine in µmol/L
Total bilirubin ≤ 1.5 x ULN (except for patients with known Gilbert's Syndrome who may have total bilirubin ≤ 3 x ULN)
ALT and AST ≤ 3 x ULN

Previous participant inclusion criteria as of 17/10/2019:
1. Newly diagnosed histologically-confirmed de-novo supratentorial glioblastoma (including gliosarcoma), by WHO guidelines with >20% surgical debulking (surgeon defined)
2. Radiotherapy to have begun within 49 days of surgery
3. Completed standard radiotherapy and concurrent temozolomide
4. Clinically appropriate for adjuvant temozolomide and capable of completing adjuvant temozolomide without dose reduction, based on investigator judgement
5. Male or female, age 18-70 years
6. Life expectancy of at least 12 weeks
7. ECOG performance status of 0-1
8. The patient is willing and able to comply with the protocol scheduled follow-up visits and examinations for the duration of the study
9. Written (signed and dated) informed consent
10. Haematological and biochemical indices within stated ranges

Previous participant inclusion criteria:
1. Newly diagnosed histologically-confirmed de-novo supratentorial glioblastoma (including gliosarcoma), by WHO guidelines with >20% surgical debulking (surgeon defined)
2. Radiotherapy to have begun within 49 days of surgery
3. Completed standard radiotherapy (60 Gray in 30 Fractions) given with concurrent temozolomide
4. Completed all planned concomitant temozolomide (75mg/m2 for 42 days) in combination with radiotherapy
5. Clinically appropriate for adjuvant temozolomide, based on investigator judgement
6. Male or female, age 18-70 years
7. Life expectancy of at least 12 weeks
8. ECOG performance status of 0-1
9. The patient is willing and able to comply with the protocol scheduled follow-up visits and examinations for the duration of the study
10. Written (signed and dated) informed consent
11. Haematological and biochemical indices within stated ranges

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
119

Key exclusion criteria
Current exclusion criteria as of 07/06/2021:
1. Pregnant or breastfeeding women or women of childbearing potential unless effective methods of contraception are used
2. Multifocal glioblastoma
3. Secondary glioblastoma (i.e. previous histological or radiological diagnosis of lower grade glioma)
4. Known extracranial metastatic or leptomeningeal disease
5. Any treatment for glioblastoma other than surgical resection/biopsy and temozolomide chemoradiotherapy
6. Dexamethasone dose >3 mg daily (or equivalent) at time of randomisation
7. Intratumoural or peritumoural haemorrhage deemed significant by the treating physician
8. Clinically relevant, active, known or suspected autoimmune disease
9. History of significant gastrointestinal impairment, as judged by the investigator
10. Any evidence of severe or uncontrolled diseases (e.g. unstable or uncompensated respiratory, cardiac, hepatic or renal disease)
11. Known hypersensitivity to trial medications or any of their excipients
12. Past medical history of interstitial lung disease, idiopathic pulmonary fibrosis, drug-induced interstitial disease which required steroid treatment or any evidence of clinically active interstitial lung disease
13. Any condition requiring systemic treatment with corticosteroids (dexamethasone 3 mg or equivalent) or other immunosuppressive medications within 14 days or randomisation. Inhaled or topical steroids, and adrenal replacement steroid doses > 10mg daily prednisolone or equivalent are permitted in the absence of active autoimmune disease
14. Treatment with any other investigational agent, or participation in another interventional clinical trial (on the interventional arm) within 28 days prior to enrolment. Participation in other interventional trials after the final IPI-GLIO visit is permitted
15. Any other active malignancy requiring treatment/whose prognosis will prevent readout from trial-endpoints, exceptions include adequately treated cone-biopsied in situ carcinoma of the cervix uteri and non-melanoma skin lesions

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1. Pregnant or breastfeeding women or women of childbearing potential unless effective methods of contraception are used
2. Multifocal glioblastoma
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11. Known hypersensitivity to trial medications or any of their excipients
12. Past medical history of interstitial lung disease, idiopathic pulmonary fibrosis, drug-induced interstitial disease which required steroid treatment or any evidence of clinically active interstitial lung disease
13. Any condition requiring systemic treatment with corticosteroids (>10 mg prednisolone daily or equivalent) or other immunosuppressive medications within 14 days or randomisation. Inhaled or topical steroids, and adrenal replacement steroid doses >10 mg daily prednisolone or equivalent are permitted in the absence of active autoimmune disease

Date of first enrolment
21/12/2018

Date of final enrolment
12/05/2021

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Mount Vernon Cancer Centre
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Study participating centre
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Study participating centre

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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
Bristol-Myers Squibb

Alternative Name(s)
Bristol-Myers Squibb Company, Bristol Myers Squibb, Bristol-Myers Company, BMS

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Funder Name
The National Brain Appeal

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

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?
Results article	protocol	26/05/2025	27/05/2025	Yes	No
Protocol article		12/03/2020	24/04/2023	Yes	No
HRA research summary	Participant information sheet		26/07/2023	No	No
Participant information sheet		11/11/2025	11/11/2025	No	Yes

Study website	Study website	11/11/2025	11/11/2025	No	Yes