

# Trial of ipilimumab immunotherapy in recently diagnosed glioblastoma brain tumours

<b>Submission date</b> 12/11/2018	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 12/11/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 27/05/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## 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>

## Contact information

### Type(s)

Scientific

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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<sup>2</sup>/day for Cycle 1 (Dose Level 0), and then 200 mg/m<sup>2</sup>/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<sup>2</sup>/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:

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). 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.

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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  $\geq 3$  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  $\geq 3$  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)  $\geq 9$  g/dL (blood transfusions not permitted to maintain haemoglobin)

Platelet count  $\geq 100 \times 10^9/L$

Absolute Neutrophil Count  $\geq 1.0 \times 10^9/L$  (G-CSF not permitted to maintain ANC)

Lymphocyte count  $\geq 0.5 \times 10^9/L$

Serum creatinine < 1.5 x ULN or a creatinine clearance of  $\geq 50$  mL/min calculated by Cockcroft-Gault formula

Female CrCl = (140-age in years) x weight in kg x 1.04 serum creatinine in  $\mu\text{mol/L}$

Male CrCl = (140-age in years) x weight in kg x 1.23 serum creatinine in  $\mu\text{mol/L}$

Total bilirubin  $\leq 1.5$  x ULN (except for patients with known Gilbert's Syndrome who may have total bilirubin  $\leq 3$  x ULN)

ALT and AST  $\leq 3$  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/m<sup>2</sup> 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 of 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

Previous exclusion criteria:

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3. Secondary glioblastoma (i.e. previous histological or radiological diagnosis of lower grade glioma)
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5. Any treatment for glioblastoma other than surgical resection/biopsy and temozolomide chemoradiotherapy
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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 (>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**

Mount Vernon Hospital

Rickmansworth Rd

Northwood

United Kingdom

HA6 2RN

**Study participating centre**

**Western General Hospital**

Edinburgh Cancer Centre

Crewe Road South

Edinburgh

United Kingdom

EH4 2XU

**Study participating centre**

**Addenbrookes Hospital**

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**Study participating centre****Guy's Hospital**

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**Study participating centre****Churchill Hospital**

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**Study participating centre****University College London Hospitals NHS Foundation Trust**

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**Study participating centre****The Christie**

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M20 4BX

**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?
<a href="#">Results article</a>		26/05/2025	27/05/2025	Yes	No
<a href="#">Protocol article</a>	protocol	12/03/2020	24/04/2023	Yes	No
<a href="#">HRA research summary</a>			26/07/2023	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes