# IDH mutated 1p/19q intact lower grade glioma following resection: Wait Or Treat? IWOT - A phase III study

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Determine whether early postoperative treatment results in a longer survival without further treatments and in the end a longer overall survival, and whether earlier treatment results in the earlier occurence of delayed adverse effects of treatment...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Nervous system neoplasms malignant and unspecified NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON48284

**Source**
ToetsingOnline

**Brief title**
IWOT

### Condition

- Nervous system neoplasms malignant and unspecified NEC

**Synonym**
astrocytoma IDH mutant, lower grade astrocytoma IDH mutant

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** European Organisation for Research in Treatment of Cancer (EORTC)
**Source(s) of monetary or material Support:** EORTC

## Intervention

**Keyword:** astrocytoma, IDH mutant, radiotherapy, temolozomide

## Outcome measures

### Primary outcome

Next intervention free survival

### Secondary outcome

Progression free survival

Overall survival

Neurological deterioration free survival

Time to deterioration of QOL

Time to deterioration of cognition

Seizure activity

Patient reported outcome

Safety profile (adverse events)

Correlation between molecular markers and outcome

In the active surveillance arm only: first intervention free survival

# Study description

### Background summary

This study aims at providing the evidence needed for the decision when to start post-operative further adjuvant treatment of patients with a grade II or an anaplastic astrocytoma, IDH mutant. These are relatively slow growing tumors that cannot be cured, and that can remain asymptomatic of oligo-symptomatic for a rather long period of time but at some point in time will become symptomatic. Radiotherapy followed by chemotherapy prolongs survival in patients with these

tumors. but these treatment are also accompanied by side effects such as fatigue and cognitive disturbances. It is unknown whether early dministration of these treatments improve the overall treatment outcome and whether the possibility of an earlier development of delayed side effects of early treatment will be balanced by a survival increase. This question when to treat is answered differently throughout the world, and has become acute again now that improved survival of adding temozolomide chemotherapy to radiotherapy has been demonstrated. It is also clear that earlier treatment may result in an earlier occurence of delayed side effects of treatment, and those side effcts may affect quality of survival. This study aims at providing the evidence needed for patients and doctors to reach an informed decision when to start postoperative treatment.

**Study objective**

Determine whether early postoperative treatment results in a longer survival without further treatments and in the end a longer overall survival, and whether earlier treatment results in the earlier occurence of delayed adverse effects of treatment

**Study design**

Phase III study, patients are randomized to either immediate postoperative treatment with radiotherapy and chemotherapy, or to a an active surveillance study arm. In this arm patients are followed according to standard guidelines every 6 months, and will undergo further treatment if tumor growth has been documented according to the treating physicians discretion.

**Intervention**

The standard of care for these tumors, radiotherapy 50.4 of 59.4 Gy (depending on the tumor grade) in fractions of 1.8 Gy,
followed by 12 cycles of temozolomide chemotherapy 150/200 mg/m2 day 1-5 every 4 weeks"

**Study burden and risks**

The burden for patients exists predominantly in the additional questionnaires and the cognitive tests that are administered at baseline and basically every 6 months thereafter. The treatment of patients is according to standard of care and brings no additional risks. Of note, there is lack of consensus at what point in time resected patients should be treated further, and what criteria should be used to guide this decision.

# Contacts

**Public**
European Organisation for Research in Treatment of Cancer (EORTC)

Av E Mounier 83/11
Brussel 1200
BE
**Scientific**
European Organisation for Research in Treatment of Cancer (EORTC)

Av E Mounier 83/11
Brussel 1200
BE

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Histologically WHO grade II (diffuse) or III (anaplastic) astrocytoma, IDHmt without 1p/19q co-deletion (local diagnosis)
At the time of randomization presence only of a non-enhancing tumor on T1 weighted contrast enhanced MR
images; some faint non-nodular enhancement or enhancement that can be ascribed to the surgical resection or
peri-operative ischemia is allowed. Preoperative enhancement is allowed provided this area is resected as shown on postoperative imaging.
Time since diagnostic surgery or first resection <= 6 months
No need for immediate radiotherapy followed by chemotherapy
Functional deficits due to the resection is allowed
Patients for whom by local judgment an active surveillance policy is a

realistic management alternative
Adults >= 18years of age
WHO PS 0-2
Adequate hematological, renal, and hepatic function
Presence of at least one paraffin block from the initial diagnosis for pathology review and translational research. If a representative FFPE block is not available, the collection of optimally 36, minimally 24 x 5 µm, unstained slides is required.
Ability to take oral medication
Written informed consent

### Exclusion criteria

Presence of signs of increased intracranial pressure after surgery
Requirement of steroids for control of tumor symptoms
Presence of uncontrolled seizures after surgery
Functional deficits due to the tumor
Presence of contra-indications for radiotherapy
Hypersensitivity to dacarbazine (DTIC), to the active substance or to any of the excipients used for TMZ capsules
Prior chemotherapy, or prior radiotherapy to the brain
Known HIV, chronic hepatitis B, or hepatitis C infection
Inability to take oral medication (e.g., frequent vomiting, partial bowel obstruction)
Concurrent severe or uncontrolled medical disease
Not pregnant, agree to use adequate birth control measures, no breast feeding
Prior or second invasive malignancy, with some defined exceptions
Presence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule;

## Study design

### Design

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| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Treatment

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 16-07-2021 |
| Enrollment: | 127 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | temozolomide |
| Generic name: | temozolomide |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 06-06-2019 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

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| Approved WMO Date: | 17-07-2019 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

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| Approved WMO Date: | 19-09-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

## Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2018-003539-31-NL |
| ClinicalTrials.gov | NCT03763422 |
| CCMO | NL68939.078.19 |