A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib in Participants With Previously Treated Glioblastoma or Other Primary Central Nervous System Tumors Harboring Activating FGFR1-3 Alterations (FIGHT-209)

Published: 22-03-2022
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Main objective: To determine the efficacy of pemigatinib in participants with recurrent GBM with an activating FGFR1-3 mutation or fusion/rearrangement. Secondary objectives: 1. To determine the efficacy of pemigatinib in participants with recurrent...

Ethical review	Approved WMO
Status	Completed
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON53632

Source
ToetsingOnline

Brief title
FIGHT-209

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor, Glioblastoma

Research involving
Human

Sponsors and support

Primary sponsor: Incyte Corporation
Source(s) of monetary or material Support: the pharmaceutical industry

Intervention

Keyword: Central Nervous System Tumors, FGFR, Glioblastoma, Phase 2

Outcome measures

Primary outcome

ORR in Cohort A, defined as the proportion of participants in Cohort A who achieve a BOR of CR or PR based on RANO as determined by an ICR.

Secondary outcome

• ORR in Cohort B, defined as the proportion of participants in Cohort B who achieve a BOR of CR or PR based on RANO as determined by an ICR.

• ORR in Cohorts A and B combined, defined as the proportion of participants in Cohorts A and B who achieve a BOR of CR or PR based on RANO as determined by an ICR.

• DOR in Cohorts A and B, respectively, defined as the time from first assessment of CR or PR until progressive disease (according to RANO and assessed by an ICR) or death (whichever occurs first).

• ORR in each cohort as determined by investigator assessment.

• DCR in Cohorts A and B, respectively, described as the proportion of participants who achieve a CR, PR, or SD as assessed by ICR.

• PFS in Cohorts A and B, respectively, defined as the time from first dose until progressive disease (according to RANO and assessed by an ICR) or death (whichever occurs first).

• OS in Cohorts A and B, respectively, defined as the time from first dose of study drug to death due to any cause.

• Safety and tolerability in each cohort, assessed by monitoring the frequency and severity of AEs by performing physical examinations, evaluating changes in vital signs and ECGs, and evaluating clinical laboratory blood samples according to NCI CTCAE v5.0.

• Impact on-study treatment, assessed by monitoring the frequency of treatment interruptions, dose reductions, and withdrawal of study treatment due to AEs.

Study description

Background summary

The recent advances in oncology have improved our understanding of the role of cancer biomarkers and led to the development of innovative drugs targeting the molecular profile of patients. Many targeted therapies are now included in treatment guidelines and have shifted clinical practice to utilize genomic information as an integral component of clinical decision-making. Molecular alterations in specific kinases can result in constitutive activity and drive initiation and progression of cancer. Biomarker-driven treatments with targeted therapies are now standard of care in certain cancers (NCCN 2021). Pemigatinib is an inhibitor of the FGFR1-3 family of receptor tyrosine kinases that is proposed for the treatment of GBM or other primary CNS tumors with an activating FGFR1-3 mutation or fusion/rearrangement. Aberrant signaling through FGFR1-3 resulting from gene mutations or chromosomal fusions/rearrangements has been demonstrated in multiple types of human cancers including CNS tumors. Fibroblast growth factor receptor signaling contributes to the development of malignancies by promoting tumor cell proliferation, survival, migration, and angiogenesis. Incyte is proposing to study pemigatinib for the treatment of GBM and other primary CNS tumors harboring an activating FGFR1-3 mutation or

fusion/rearrangement.

Study objective

Main objective: To determine the efficacy of pemigatinib in participants with recurrent GBM with an activating FGFR1-3 mutation or fusion/rearrangement.

Secondary objectives:
1. To determine the efficacy of pemigatinib in participants with recurrent GBM or other recurrent gliomas, circumscribed astrocytic gliomas, and glioneuronal and neuronal tumors with an activating FGFR1-3 mutation or fusion/rearrangement.
2. To determine the safety and tolerability of pemigatinib in participants with recurrent GBM or other recurrent gliomas, circumscribed astrocytic gliomas, and glioneuronal and neuronal tumors, with an activating FGFR1-3 mutation or fusion/rearrangement.

Study design

This is an open-label, monotherapy study of pemigatinib in participants with recurrent GBM or other primary CNS tumors with an activating FGFR1-3 mutation or fusion/rearrangement. This study consists of 3 cohorts, Cohorts A, B, and C, and will enroll approximately 82, 82, and 25 participants into each cohort, respectively. Participants will receive pemigatinib 13.5 mg QD on a 2-week on-therapy and 1-week off-therapy schedule as long as they are receiving benefit and have not met any criteria for study withdrawal. Participants with local laboratory test results documenting an activating FGFR1, FGFR2, or FGFR3 mutation or gene fusion/rearrangement are eligible to enroll as long as the results meet the cohort criteria. Confirmatory testing through the sponsor-designated central genomics laboratory will be performed for all participants; however, results from the central genomics laboratory are not required before enrollment.

Intervention

This study consists of 3 cohorts, Cohorts A, B, and C, and will enroll approximately 82, 82, and
25 participants into each cohort, respectively. Participants will receive pemigatinib 13.5 mg QD on a 2-week on-therapy and 1-week off-therapy schedule as long as they are receiving benefit and have not met any criteria for study withdrawal.

Study burden and risks

Participating in the study can have the following disadvantages:
- Participants may experience side effects or adverse effects such as:
- Increased phosphorus in blood,

- diarrhea,
- hair loss and/or thinning,
- fatigue,
- dry mouth redness and/or sores in the mouth and/or throat,
- constipation,
- taste alteration,
- nausea,
- decreased appetite,
- anemia
- Participants may suffer from the measurements during the study. For example: a blood draw can be painful. Or Participants could get bruising as a result.
- Participating in the study costs extra time.
- Participants must adhere to the agreements associated with the study.
- The questionnaires can be confronting.
- Participants must adhere to strict rules about taking drugs.
- There could be disadvantages for the participants* partner of housemate.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Ability to comprehend and willingness to sign a written ICF for the study. For Germany: Only participants who can provide their own consent are able to participate in this clinical study.
2. Male and female participants aged 18 years or older at the time of signing the ICF.
3. Histological, cytological, or molecular confirmation of recurrent GBM or other gliomas, circumscribed astrocytic gliomas, and glioneuronal or neuronal tumors that have recurred.
a. For Cohort A: Prior, histopathologically proven, WHO Grade 4, IDH* wild-type GBM OR molecular diagnosis of IDH-wild-type, diffuse astrocytic glioma with molecular features of Grade 4 GBM per WHO 2021 (astrocytic glioma requires presence of either amplification of EGFR,whole chromosome 7 gain and whole chromosome 10 loss, or TERT promoter mutation) that has recurred or progressed on or after treatment with at least 1 line of standard-of-care therapy.
b. For Cohort B: Prior, histopathologically proven, per WHO criteria, gliomas other than GBM (eg, IDH-mutant astrocytoma, IDH-mutant and 1p/19q codeleted oligodendroglioma), circumscribed astrocytic gliomas, and glioneuronal and neuronal tumors that are recurrent or have progressed on or after at least 1 line of standard-of-care therapy (eg, radiotherapy and/or treatment with an alkylating chemotherapy such as TMZ, CCNU, or BCNU-containing chemotherapy).
4. Radiographically measurable disease (per RANO). Tumor lesions located in a previously irradiated area, or in an area subjected to other loco-regional therapy, are considered measurable if progression has been clearly demonstrated in the lesion.
5. Karnofsky performance status >= 60.
6. Life expectancy >= 12 weeks.
7. Documentation of an actionable FGFR1-3 gene alteration (defined mutations, gene fusion/rearrangements, or in-frame deletions) from tissue or cfDNA from a qualified laboratory such as FMI or Guardant Health may be acceptable after review by medical monitor. Participants with known FGFR resistance mutations are not eligible.
a. Cohort A: Participants with histopathologically proven, WHO Grade 4, IDH*wild-type GBM OR molecular diagnosis of IDH-wild-type, diffuse astrocytic glioma with molecular features of Grade 4 GBM per WHO 2021 (astrocytic glioma requires presence of either amplification of EGFR, whole chromosome 7 gain and whole chromosome 10 loss, or TERT promoter mutation) that are recurrent, harboring FGFR1-3 fusions/or other rearrangements (FGFR1-3 in-frame fusions, any FGFR2 rearrangement, or FGFR1/3 rearrangement with known partner) or with a

defined FGFR1-3 activating mutation or in-frame deletion. Only participants with FGFR fusions or rearrangements with an intact kinase domain are eligible.
b. Cohort B: Participants with other histopathologically proven, per WHO criteria, gliomas other than GBM (eg, IDH-mutant astrocytoma, IDHmutant and 1p/19q codeleted oligodendroglioma), circumscribed astrocytic gliomas, and glioneuronal and neuronal tumors that are recurrent, harboring FGFR1-3 fusions/or other rearrangements (FGFR1-3 in-frame fusions, any FGFR2 rearrangement, FGFR1/3 rearrangement with known partner) or with a defined FGFR1-3 activating mutation or in-frame deletion. Only FGFR fusions or rearrangements with an intact kinase domain are eligible.
8. MRI-documented objective progression after prior therapy and must have no therapy available that is likely to provide clinical benefit. An interval of at least 12 weeks after prior radiotherapy is required unless there is either histopathological confirmation of recurrent tumor or new enhancement on MRI outside the radiotherapy field. Participants who are intolerant of or unsuitable for the approved therapy, in the opinion of the investigator, are eligible only if they have no therapy available that is likely to provide clinical benefit.
9. Most recent archival tumor specimen must be a tumor block or a minimum of 15 unstained slides from biopsy or resection of primary tumor or metastasis.

Exclusion criteria

1. Prior receipt of a selective an FGFR inhibitor.
2. Receipt of anticancer medications or investigational drugs for any indication or reason within 28 days before first dose of study drug. Participants must have recovered (<= Grade 1) from AEs from previously administered therapies.
3. Participants may have had treatment for an unlimited number of prior relapses but must not have had prior bevacizumab or other VEGF/VEGFR inhibitors.
4. Concurrent anticancer therapy.
5. Candidate for potentially curative surgery.
6. Dexamethasone (or equivalent) > 4 mg daily at the time of study registration (higher dose of steroid for symptom control is allowed during the study).
7. Current evidence of clinically significant corneal or retinal disorder as confirmed by ophthalmologic examination.
8. Diffuse leptomeningeal disease.
9. Radiation therapy administered within 12 weeks before enrollment/first dose of study drug. An interval of at least 12 weeks after prior radiotherapy is required unless there is either histopathological confirmation of recurrent tumor or new enhancement on MRI outside the radiotherapy field.
10. Known additional malignancy that is progressing or requires active systemic treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone

potentially curative therapy.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	16-05-2023
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pemazyre
Generic name:	Pemigatinib

Ethics review

Approved WMO Date:	22-03-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-06-2022
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2021-004740-24-NL
ClinicalTrials.gov	NCT05267106
CCMO	NL80185.056.22

Study results

Date completed: 09-12-2024

Summary results
Trial ended prematurely