Phase 3b Study for Management of Ocular Side Effects in Subjects with EGFR-Amplified Glioblastoma Receiving Depatuxizumab Mafodotin (ABT-414)

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Eye disorders NEC
Study type	Interventional

Summary

ID

NL-OMON48749

Source
ToetsingOnline

Brief title
M16-534

Condition

- Eye disorders NEC
- Nervous system neoplasms malignant and unspecified NEC

Synonym
eye disorders, Glioblastoma

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie Deutschland GmbH & Co. KG
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: Brain tumor, Glioblastoma

Outcome measures

Primary outcome

The primary endpoint is defined as the percentage of subjects with either a >= 3-line decline from baseline (>= + 0.3 on LogMAR scale) in visual acuity (with baseline correction), or >= Grade 3 OSE severity on the Corneal Epithelial Adverse Event (CEAE) scale, either of which will indicate inadequate control of OSEs requiring a change in OSE management strategy.

Unless otherwise noted, visual acuity will be measured using baseline correction, which will be determined at the screening ophthalmology visit and used to assess visual acuity at all remaining ophthalmology visits, for measuring changes in visual acuity and for determining the visual acuity component of the primary endpoint. Details on determining baseline correction are provided in the operations manual.

The primary endpoint will be assessed over 8 weeks after initiation of depatuxizumab mafodotin treatment.

Secondary outcome

The Logarithm of the Minimum Angle of Resolution (LogMAR) scale is used to measure visual acuity. The CEAE scale will be used to measure the severity of OSEs. These will be followed over the course of treatment.

Study description

Background summary

Depatuxizumab mafodotin is being investigated in late phase clinical trials of patients with glioblastoma (GBM) that demonstrate epidermal growth factor receptor (EGFR) amplification. The dose-limiting toxicities (DLTs) observed after depatuxizumab mafodotin exposure have been limited to ocular side effects (OSEs). This exploratory study is designed to evaluate several depatuxizumab mafodotin-related OSE management strategies.

Study objective

This exploratory study is designed to evaluate several depatuxizumab mafodotin-related OSE management strategies.

The main objective of this trial is to estimate the percentage of subjects in each prophylactic treatment arm who require a change in Ocular Side Effects (OSE) management due to inadequate control of Ocular Side Effects.

The secondary objective of this trial is to assess the effects of intervention with bandage contact lenses (BCL) on visual acuity and OSE symptom severity for those subjects who require intervention due to inadequate control of OSEs.

Study design

This is a Phase 3b open-label, randomized study. All subjects will receive depatuxizumab mafodotin treatment in addition to current standard-of-care treatment of concomitant radiation therapy/temozolomide (RT/TMZ) and adjuvant TMZ. Subjects will be randomized 1:1:1 to one of the 3 opthalmologic prophylactic treatment arms.

Intervention

Subjects will receive depatuxizumab mafodotin during the chemoradiation phase (consisting of radiation and temozolomide [RT/TMZ]) and depatuxizumab mafodotin during adjuvant therapy with TMZ. Depatuxizumab mafodotin will be administered every 2 weeks during standard 6-week RT/TMZ therapy, followed by a 4-week recovery period. During adjuvant therapy, depatuxizumab mafodotin will be administered every 2 weeks for 12 cycles (28 days/cycle).

Subjects will be randomized to one of 3 prophylactic ophthalmologic treatments (Standard Steroids, Standard Steroids/Vasoconstrictors, or Enhanced Steroids/Vasoconstrictors).

Study burden and risks

The subjects participating in the study will have a higher burden because of participation in the trial. Subject will be visiting the hospital more frequently. During these visits study procedures will be performed including blood and urine sampling, ophthalmology exam, physical exam, vital signs and filling in questionnaires. Subject will also be tested for significant heart conditions and pregnancy.
Next to this the subjects will receive Depatux-M and prophylactic eye treatment in additional to the standard treatment.

Risks in this study include adverse events from Depatux-M and the prophylactic eye treatment and adverse events related to the standard treatment (radiation treatment and TMZ). Depatux-M has been tested in a limited number of people, so the side effects are only partially known. Eye problems are the main side effects caused by Depatux-M. Other most frequently reported side effects (>= 10% of all studies reported) in Depatux-M studies were: fatigue or decreased energy, decreased appetite, headache and changes in the blood tests that show possible liver damage. Steroid eye drops used as part of the prophylactic eye treatments can increase pressure in the eye, which over time could lead to visual impairment, and increase the risk of eye infections.

The current data of Depatux-M and the lack of an effective treatment alternative reflect an acceptable rationale and risk for treating adult patients with cancer that has a moderate to high level of EGFR expression with Depatux-M in the context of a clinical trial.

Contacts

Public
AbbVie Deutschland GmbH & Co. KG

Wegalaan 9
Hoofddorp 2132 JD
NL
Scientific
AbbVie Deutschland GmbH & Co. KG

Wegalaan 9
Hoofddorp 2132 JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Participant has a histologically proven, World Health Organization (WHO) grade IV glioblastoma or WHO grade IV gliosarcoma.;• Tumors must demonstrate epidermal growth factor receptor (EGFR) amplification.;• Tumors must be supratentorial in location.;• Participant must have recovered from the effects of surgery, postoperative infection, and other complications; has no significant post-operative hemorrhage.;• Participant has a Karnofsky performance status (KPS) of 70 or higher.;• Participant has adequate bone marrow, renal, and hepatic function.;• Electrocardiogram without evidence of acute cardiac ischemia <= 21 days prior to randomization.;• Participant has a life expectancy of >= 3 months;•Participant has infection with hepatitis B virus (i.e., hepatitis B surface antigen) or hepatitis C virus (i.e., positive for hepatitis C antibody).
Subjects who have a history of hepatitis C who have documented cures after anti-viral therapy may be enrolled. Subjects with confirmed
positive test result for human immunodeficiency virus (HIV), with CD4 count < 200 cells/microliter are excluded. Note that subjects who are HIV positive are eligible, provided they are under treatment with highly active antiretroviral therapy (HAART) and have a CD4 count >= 200 cells/microliter within 30 days prior to registration, as the treatments involved in this protocol may be significantly immunosuppressive.

Exclusion criteria

• Participants with newly diagnosed Glioblastoma: has received prior chemotherapy or radiotherapy for cancer of the head and neck region; has received prior treatment with Gliadel wafers or any other intratumoral or intracavitary treatment.;• Participant has hypersensitivity to any component of Temozolomide or dacarbazine.;• Participant has received anti-cancer therapy (including chemotherapy, immunotherapy, radiotherapy, hormonal, biologic, or any investigational therapy) prior to 5 years of Study Day 1.;• Participant has clinically significant uncontrolled condition(s) as described in the protocol.;•

Participant has any medical condition which in the opinion of the investigator places the participant at an unacceptably high risk for toxicities.;• Participant has had another active malignancy within the past 3 years except for any cancer considered cured or non-melanoma carcinoma of the skin.;• Participant has a history of herpetic keratitis.;• Participant is not suitable for receiving ocular steroids with conditions as described in the protocol.;• Participant has had laser-assisted in situ keratomileusis (LASIK) procedure within the last 1 year or cataract surgery within the last 3 months.;• Participant has a visual condition that compromises the ability to accurately measure visual acuity or assess visual activities of daily living (vADLs).;• Participant has infection with hepatitis B virus (i.e., hepatitis B surface antigen) or hepatitis C virus (i.e., positive for hepatitis C antibody). Subjects who have a history of hepatitis C who have documented cures after anti-viral therapy may be enrolled. Subjects with confirmed
positive test result for human immunodeficiency virus (HIV), with CD4 count < 200 cells/microliter are excluded. Note that subjects who are
HIV positive are eligible, provided they are under treatment with highly active antiretroviral therapy (HAART) and have a CD4 count >= 200
cells/microliter within 30 days prior to registration, as the treatments involved in this protocol may be significantly immunosuppressive.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	9
Type:	Anticipated

Medical products/devices used

Product type:	Medicine

Brand name:	Depatuxizumab Mafodotin
Generic name:	Depatuxizumab Mafodotin

Ethics review

Approved WMO Date:	16-04-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	28-08-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	19-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-10-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-11-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-12-2018
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	13-02-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-06-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2017-003171-64-NL
ClinicalTrials.gov	NCT03419403
CCMO	NL64716.041.18

Study results

Results posted: 17-02-2021

Summary results
Trial never started

First publication
16-02-2021