Dose Finding Study of [177Lu]Lu-NeoB in Newly Diagnosed Glioblastoma and in Recurrent Glioblastoma

Last Update: May 21, 2025
Phase Ib Dose Finding Study Assessing Safety and Activity of [177Lu]Lu-NeoB in Combination With Radiotherapy and Temozolomide in Subjects With Newly Diagnosed Glioblastoma and as a Single Agent in Recurrent Glioblastoma
ClinicalTrials.gov Identifier:
NCT05739942
Novartis Reference Number:CAAA603C12101
See if you Pre-qualify
All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

This study will investigate different doses of \[177Lu\]Lu-NeoB in combination with RT and TMZ in participants with newly diagnosed glioblastoma, with methylated or unmethylated promoter, to assess the safety and efficacy of \[177Lu\]Lu-NeoB in combination with the SoC and in recurrent glioblastoma as single agent, to identify the recommended dose and to also explore the safety of the PET imaging agent \[68Ga\]Ga-NeoB and characterize its uptake in the tumor area. Newly diagnosed glioblastoma:

Glioblastoma is the most common and aggressive type of primary brain tumor, with a high mortality rate. The current standard of care (SoC) in newly diagnosed glioblastoma includes the combination of the alkylating agent Temozolomide (TMZ) with Radiotherapy (RT). The hypothesis of this study is to improve the outcome for participants by combining the current standard of care with the radioligand therapy \[177Lu\]Lu-NeoB. Participants with newly diagnosed glioblastoma enrolled into this trial will be treated with the standard regimen TMZ and RT, combined with \[177Lu\]Lu-NeoB every 4 weeks (Q4W) for 6 administrations. In cases where participants tolerate and benefit from \[177Lu\]Lu-NeoB, they can receive an additional 4 doses (total up to 10 dose administrations). During this period, regular safety and efficacy assessments are planned on a weekly basis. The primary objective of this trial is to identify the recommended dose of \[177Lu\]Lu-NeoB in combination with TMZ and RT in participants with newly diagnosed glioblastoma and to characterize the safety and tolerability of this treatment. For this reason, participants will be enrolled and treated in cohorts with increasing dose levels and the totality of available data will be used to define the recommended dose. Contrast enhanced MRI assessments are to be repeated every 8 weeks. Following treatment, all participants will be followed for up to 5 additional years for safety, progression of disease and survival. Participants with newly diagnosed glioblastoma will undergo a baseline \[68Ga\]Ga-NeoB PET/CT or PET/MRI after the surgery/biopsy of the tumor.

Recurrent glioblastoma:

Participants with recurrent glioblastoma carry a dismal prognosis and a short survival. The primary objective in

recurrent glioblastoma is to determine the recommended dose of \[177Lu\]Lu-NeoB as single agent and to characterize the safety and tolerability of this treatment. For this reason, participants will be enrolled and treated in cohorts with increasing dose levels and the totality of available data will be used to define the recommended dose. In this study, all participants with recurrent glioblastoma will undergo \[68Ga\]Ga-NeoB PET scan to assess GRPR expression during the screening period. \[177Lu\]Lu-NeoB will be administered as a single dose every 3 weeks (Q3W) for 6 administrations. Up to 4 additional administrations of \[177Lu\]Lu-NeoB may be considered if participants tolerate and benefit from \[177Lu\]Lu-NeoB (total up to 10 dose administrations).

Condition
Newly Diagnosed and Recurrent Glioblastoma
Phase
Phase1
Overall Status
Recruiting
Number of Participants
48
Start Date
May 15, 2024
Completion Date
Aug 28, 2031
Gender
All
Age(s)
18 Years - 100 Years (Adult, Older Adult)

Interventions

Other

Temozolomide

Capsules/ lyophilized powder in single-dose vial for reconstitution.
Drug

[177Lu]Lu-NeoB

Radiopharmaceutical solution for infusion
Drug

[68Ga]Ga-NeoB

Either provided as Kit for the radiopharmaceutical preparation of \[68Ga\]Ga-NeoB or as ready to use radiopharmaceutical solution for injection

Eligibility Criteria

Key Inclusion Criteria/Common Criteria (Group 1 - Newly diagnosed glioblastoma, Group 2 - Recurrent glioblastoma):

1. Signed informed consent must be obtained prior to participation in the study
2. Age \>= 18 years
3. Histologically confirmed glioblastoma according to WHO classification established following either a surgical resection or biopsy
4. Participants who are receiving corticosteroid treatment with dexamethasone, must be treated with a dose of =\<4 mg/day (or other corticosteroids at equivalent dose) for a minimum of 7 days before initiation of study treatment
5. Adequate bone marrow and organ function as defined by the following laboratory values obtained prior to receiving the first study treatment:

1. Absolute Neutrophil Count (ANC) \>= 1.5 x 10\^9/L
2. Platelet count \>= 100 x 10\^9/L
3. Hemoglobin \>= 10.0 g/dL
4. Creatinine clearance \>= 60 mL/min calculated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) creatinine equation .
5. Aspartate transaminase (AST) or Alanine transaminase (ALT) =\< 3.0 x ULN
6. Total bilirubin (TBIL) \< 1.5 × ULN (any elevated bilirubin should be asymptomatic at enrollment) except for participants with Gilbert's syndrome who may only be included if the total bilirubin is =\< 3.0 × ULN or direct bilirubin =\< 1.5 × ULN
7. Serum lipase ≤ 1.5 x ULN. For serum lipase \> ULN - =\< 1.5 x ULN, value must be considered not clinically significant and not associated with risk factors for acute pancreatitis

Key Inclusion Criteria/Newly diagnosed glioblastoma (Group 1):

9. Availability of tumor tissue representative of glioblastoma from definitive surgery or biopsy, to support biomarker analysis 10. Presence of gadolinium enhancement at the tumor region in the pre-surgery MRI

Key Inclusion Criteria/Recurrent glioblastoma (Group 2) 11. Presence of \[68Ga\]Ga-NeoB uptake by PET/CT or PET/MRI at the tumor region 12. Having first or second glioblastoma recurrence, after standard therapy that includes prior radiation therapy (RT) and at least 12 weeks from completion of RT 13. Evidence of recurrent disease (RD) demonstrated by disease progression using modified Response Assessment in Neuro-Oncology (mRANO) criteria. RD must be documented with at least one bi-dimensionally measurable contrast-enhancing lesion with clearly defined margins by MRI scan, with minimal diameters of 10 mm, according to mRANO criteria. For those participants who will undergo a second surgery for recurrence, pre-surgery MRI will be used for confirmation of RD.

14. If a second surgery is performed for glioblastoma recurrence, the following criteria must be met:

1. residual and measurable disease post-surgery is not required but surgery must have confirmed the recurrence diagnosis by MRI.
2. surgery completed at least 2 weeks prior to study treatment initiation, with post-surgery recovery without any complications related to surgical procedure.

Key Exclusion Criteria/Common Criteria (Group 1 - Newly diagnosed glioblastoma, Group 2 - Recurrent glioblastoma):

1. Additional, concurrent, or active therapy for glioblastoma outside of the present study 4. History or current diagnosis of impaired cardiac function, clinically significant cardiac disease, or ECG abnormalities indicating significant risk of safety for study participants such as:

a. Documented myocardial infarction (MI), angina pectoris, cardiomyopathy, symptomatic pericarditis, or

coronary artery bypass graft (CABG) within 6 months prior to study entry b. Long QT syndrome or family history of idiopathic sudden death or congenital long QT syndrome, or any of the following: i. Risk factors for Torsade de Pointes (TdP) including uncorrected hypocalcemia, hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia ii. Concomitant medication(s) with a known risk to prolong the QT interval and/or known to cause Torsade de Pointes that cannot be discontinued or replaced by safe alternative medication (e.g., within 5 half-lives or 7 days prior to starting study drug) iii. Inability to determine the Fridericia QT correction formula (QTcF) interval c. Clinically significant cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third-degree AV block) d. Resting QTcF \>= 450 msec (male) or \>= 460 msec (female) e. Left Ventricular Ejection Fraction (LVEF) \<50% as determined by echocardiogram (ECHO) or Multiple Gated Acquisition (MUGA) scan f. Uncontrolled hypertension defined by a Systolic Blood Pressure (SBP) \>=160 mmHg and/or Diastolic Blood Pressure (DBP) \>=100 mm Hg, with or without anti-hypertensive medication.

5. History of another active malignancy in the previous 3 years prior to study entry, except participants with prior history of superficial bladder cancer, any in situ carcinoma or basal or squamous cell skin cancer treated curatively

Key Exclusion Criteria/Newly diagnosed glioblastoma (Group 1):

17. Any prior treatment for glioma of any grade, including: prolifeprospan 20 with carmustine wafer, intracerebral agent, radiation treatment, chemotherapy or immunotherapy

Key Exclusion Criteria/Recurrent glioblastoma (Group 2) 18. Previous treatment with bevacizumab for the treatment of glioblastoma with therapeutic intent, or with bevacizumab as supportive therapy (e.g., edema reduction) within 60 days of initiation of study treatment 19. More than two prior lines of systemic therapy, more than one surgical resection for recurrent disease and treatment with an intracerebral/intracranial agent prior to starting \[177Lu\]Lu-NeoB. Administration in adjuvant setting counts as a line of prior systemic treatment.

France

Novartis Investigative Site

Recruiting

Dijon,Cote D Or,21034,France

Novartis Investigative Site

Recruiting

Marseille,13885,France

Germany

Novartis Investigative Site

Recruiting

Essen,45147,Germany

Novartis Investigative Site

Recruiting

Koeln,50937,Germany

Novartis Investigative Site

Recruiting

Muenchen,80377,Germany

Novartis Investigative Site

Recruiting

Rostock,18057,Germany

Israel

Novartis Investigative Site

Recruiting

Jerusalem,9112001,Israel

Italy

Novartis Investigative Site

Recruiting

Reggio Emilia,RE,42123,Italy

Portugal

Novartis Investigative Site

Recruiting

Porto,4200-072,Portugal

Spain

Novartis Investigative Site

Recruiting

Granada,Andalucia,18014,Spain

Novartis Investigative Site

Recruiting

Madrid,28009,Spain

Novartis Investigative Site

Recruiting

Madrid,28040,Spain

Novartis Investigative Site

Recruiting

Badalona,Catalunya,08916,Spain

Novartis Investigative Site

Recruiting

Hospitalet de LLobregat,Catalunya,08907,Spain

United States

University Hospitals Cleveland Medical Center

Recruiting

Cleveland,Ohio,44106-5028,United States

Heather Buck

Phone: 216-844-7164
Email: Heather.Buck@UHhospitals.org

Prashant Vempati

Dana Farber Cancer Institute

Recruiting

Boston,Massachusetts,02215,United States

Elisa Aquilanti

Amanda Dresser

Email: amanda_dresser@dfci.harvard.edu

University of California LA

Recruiting

Los Angeles,California,90095,United States

David Sennung

Email: dsennung@mednet.ucla.edu

Timothy F Cloughesy

Uni of Utah Huntsman Cancer Inst

Recruiting

Salt Lake City,Utah,84103,United States

Dallin Toews

Phone: 801-587-0272
Email: dallin.toews@hci.utah.edu

Howard Colman

Memorial Sloan Kettering Cancer Ctr

Recruiting

New York,New York,10065,United States

Alexandru Ionescu

Phone: 212-639-3854
Email: ionesca1@mskcc.org

Brandon Imber

University of Colorado Denver

Recruiting

Aurora,Colorado,80045,United States

Denise Damek

John Richter

Email: john.richter@cuanschutz.edu

Worldwide Contacts

If the location of your choosing does not feature any contact detail, please reach out using the information below.

Novartis Pharmaceuticals

Phone: +41613241111

Email: novartis.email@novartis.com

Novartis Pharmaceuticals

Phone: 1-888-669-6682
Email: novartis.email@novartis.com

Source URL: *https://prod1.novartis.com/clinicaltrials/study/nct05739942*

List of links present in page

1. https://clinicaltrials.gov/ct2/show/NCT05739942
2. #trial-eligibility
3. tel:216-844-7164
4. mailto:Heather.Buck@UHhospitals.org
5. mailto:amanda_dresser@dfci.harvard.edu
6. mailto:dsennung@mednet.ucla.edu
7. tel:801-587-0272
8. mailto:dallin.toews@hci.utah.edu
9. tel:212-639-3854
10. mailto:ionesca1@mskcc.org
11. mailto:john.richter@cuanschutz.edu
12. tel:+41613241111
13. mailto:novartis.email@novartis.com
14. tel:1-888-669-6682
15. mailto:novartis.email@novartis.com