A Phase 1b/2, open-label dose escalation with expansion study of GB5121 in adult patients with relapsed/refractory primary or secondary central nervous system lymphoma or primary vitreoretinal lymphoma, with a Phase 2 open-label single dose level study of GB5121 in adult patients with relapsed/refractory primary central nervous system lymphoma

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Phase 1b Dose Escalation Objectives • To determine the safety and tolerability of escalating doses of GB5121• To determine the optimal biological dose (OBD) and/or maximum tolerated dose (MTD), and recommended Phase 2 dose (RP2D) of GB5121 Phase 1b...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Nervous system neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON53713

Source
ToetsingOnline

Brief title
GB5121-2101 STAR CNS

Condition

- Nervous system neoplasms benign

Synonym
cancer of the central nervous system, lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: GB005, Inc., a wholly-owned subsidiary of Gossamer Bio, Inc.
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: central nervous system, GB5121, lymphoma

Outcome measures

Primary outcome

Phase 1b Dose Escalation Objectives

• Incidence of AEs, DLTs, and SAEs

• OBD and/or MTD and RP2D of GB5121

Phase 1b Expansion Objectives

• Incidence of AEs and SAEs

Phase 2 Objectives

• ORR according to the IPCG criteria by Blinded Independent Central Review

(BICR) Committee

Secondary outcome

Phase 1b Expansion Objectives

• ORR according to the International Primary CNS Lymphoma Collaborative Group

(IPCG) criteria by Investigator Assessment

Phase 2 Objectives

• Duration of Response (DOR) by BICR Committee

Study description

Background summary

Central nervous system (CNS) lymphoma is a non-Hodgkin lymphoma in which malignant cells are present in the brain and/or spinal cord. CNS lymphoma is highly aggressive and prognosis remains poor despite improvements in treatments in the front-line setting.
As there is no uniform standard-of-care treatment available to date, participation in clinical trials is encouraged. New safe and effective treatments are urgently needed.
GB5121 is a selective, irreversible small molecule inhibitor of Bruton*s tyrosine kinase (BTK) that is CNS penetrant, and inactivates BTK providing a potential treatment option in BTK-driven cancers and other diseases (such as CNS lymphoma).
To date there are no prior human studies with the study treatment yet conducted; a Phase 1 study in healthy volunteers is ongoing. Currently the study treatment demonstrated a favorable nonclinical profile with minimal toxicology findings.

Study objective

Phase 1b Dose Escalation Objectives
• To determine the safety and tolerability of escalating doses of GB5121
• To determine the optimal biological dose (OBD) and/or maximum tolerated dose (MTD), and recommended Phase 2 dose (RP2D) of GB5121

Phase 1b Expansion Objectives
• To determine the safety and tolerability of the RP2D of GB5121

Phase 2 Objectives
• To assess objective response rate (ORR) according to International Primary CNS Lymphoma Collaborative Group (IPCG) criteria

Study design

This is a Phase 1b/2 open-label, multicenter, multinational dose escalation with expansion study of GB5121 in adult patients with r/r PCNSL or SCNSL or PVRL, with a Phase 2 open-label single dose level study of GB5121 in adult patients with r/r PCNSL.

Intervention

Phase 1b (Dose Escalation and Expansion)
In Phase 1b Dose Escalation, the expected starting dose of GB5121 is 10 mg twice daily (BID).
In the Phase 1b Expansion, the dose of GB5121 administered will be the RP2D established from the Phase 1b Dose Escalation.

Phase 2
GB5121 at the RP2D from Phase 1b Dose Escalation.

Study burden and risks

Risks which are associated with the study drug and procedures are described in details in the main patient Information sheet and
informed consent form.

Contacts

Public
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Science Park Road 3013
San Diego CA 92121
US
Scientific
GB005, Inc., a wholly-owned subsidiary of Gossamer Bio, Inc.

Science Park Road 3013
San Diego CA 92121
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Phase 1b Dose Escalation and Expansion:
1. Patients who are at least 18 years of age at the time of signing the informed consent form (ICF) prior to initiation of any study specific activities/procedures.
2. Patients must have histologically/cytologically confirmed PCNSL, primary vitreoretinal lymphoma (PVRL), or CNS-only involvement of a systemic B-cell lymphoma.
3. All patients must have relapsed/refractory disease and must have received all possible standard-of-care CNS-directed treatment regimens or patients for which further standard-of-care treatment options are contraindicated or declined.
4. Patients must be able to tolerate gadolinium-enhanced MRI scans, or contrast-enhanced CT .
5. Patients with parenchymal lesions must have baseline imaging (gadolinium-enhanced MRI or if contraindicated, contrast-enhanced CT, of the brain) within 28 days prior to first study drug dose. For patients with leptomeningeal disease only, CSF cytology must document lymphoma cells and/or imaging findings consistent with leptomeningeal disease after informed consent and prior to first study dose (at the discretion of the Investigator).
6. Patients with parenchymal lesions must have measurable disease (disease that has at least one lesion >= 10 mm in the longest diameter) on imaging (gadolinium-enhanced MRI or if contraindicated, contrast-enhanced CT, of the brain) prior to first study dose.
7. Patients must be able to tolerate and consent for a lumbar puncture and/or have pre-existing placement of an Ommaya reservoir, unless clinically contraindicated.
8. Patients must have recovered to <= Grade 1 toxicity from prior therapy.
9. Patients, when available, should be able to submit at minimum 3 and up to 20 unstained formalin-fixed, paraffin-embedded (FFPE) slides from the initial tissue diagnosis, preferably prior to study enrollment.
10. Patients must have a performance status of 0, 1, or 2 on the Eastern Cooperative Oncology Group (ECOG) Performance Scale.

11. Demonstrate adequate bone marrow and organ function as defined in the protocol. All screening laboratories for organ functions should be performed within 14 days of initiating the study drug.
12. Female patients must be:
a. Of non-childbearing potential: Evidence of post-menopausal status. Refer to Appendix 4 (Section 10.4) for definitions; or
b. If of childbearing potential, patient must use a highly effective method of contraception for the duration of treatment and for at least 30 days following the last dose of GB5121. Refer to Appendix 4 (Section 10.4) for contraception guidance.
c. Female patients of childbearing potential must have a negative serum or urine pregnancy test within 72 hours prior to receiving the first dose of study drug.
13. Male patients who are not abstinent who are partners of women of childbearing potential must use 2 highly effective method of contraception throughout the entire study period. Refer to Appendix 4 (Section 10.4) for contraception guidance. Those with partners using hormonal contraceptives must also be using an additional approved method of contraception (as described previously).
14. Male and female patients must refrain from donating sperm or eggs from informed consent through at least 30 days after last dose of GB5121 for females and 90 days for males.
15. Patients provide written informed consent for the study which includes compliance with the requirements and restrictions listed in the ICF and in this protocol.

Phase 2: criteria specific to phase 2, the remaining criteria are identical with phase1b, criteria 7 is not applicable
2. Patients with histologically/cytologically confirmed PCNSL.
5. Patients with parenchymal lesions must have baseline imaging (gadolinium-enhanced MRI or if contraindicated, contrast-enhanced CT, of the brain) after informed consent and prior to first study drug dose. For subjects with leptomeningeal disease only, CSF cytology must document lymphoma cells and/or imaging findings consistent with leptomeningeal disease after informed consent and prior to first study dose (at the discretion of the Investigator).

Exclusion criteria

Phase 1b Dose Escalation and Expansion:
1. Patients are concurrently using other approved or investigational antineoplastic agents.
2. Patients have an active concurrent malignancy requiring active therapy.
3. Patients are allergic to components of the study drug (Section 5.1).
4. Patients have a known bleeding diathesis (eg, von Willebrand's disease) or hemophilia.

5. Patients who require therapeutic anticoagulation, including dual antiplatelet agents. Patients who have received therapeutic anticoagulation, including dual antiplatelet agents, within 5 half-lives of the anticoagulant, or 14 days, whichever is longer, prior to starting the study drug. Patients who require the use of antiplatelet agents should be discussed with the Sponsor's Medical Monitor.
6. Patients have significant abnormalities on screening electrocardiogram (ECG) and active and significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure, uncontrolled hypertension, valvular disease, pericarditis, or myocardial infarction within 6 months of screening.
7. Patients with any of the following will be excluded:
a. A marked baseline prolongation of QT/QTc interval (eg, repeated demonstration of a QTc interval > 480 ms [CTCAE grade 2]) using Frederica's QT correction formula.
b. A history of additional risk factors for Torsades de Pointes (eg, heart failure, hypokalemia, family history of long QT syndrome).
c. The use of concomitant medications that prolong the QT/QTc interval (Section 10.6).
8. Patients are known to have a history of active or chronic infection with hepatitis C virus (HCV), hepatitis B virus (HBV), as determined by serologic tests.
9. Known history of infection with HIV.
10. Patients are known to have an uncontrolled active infection.
11. Patients have a history of stroke or intracranial hemorrhage within 6 months prior to enrollment.
12. Patients have a life-threatening illness, medical condition, or organ system dysfunction that, in the opinion of the Investigator, could compromise the patient's safety or put the study outcomes at undue risk.
13. Patients have an inability to swallow capsules or tablets, or disease significantly affecting gastrointestinal function and/or inhibiting small intestine absorption (including malabsorption syndrome, resection of the small bowel, or poorly controlled inflammatory bowel disease).
14. Women who are pregnant or nursing (lactating).
15. Patients have received chemotherapy, monoclonal antibodies, or targeted anticancer therapy within <= 2 weeks or 5 half-lives, whichever is longer, prior to starting the study drug, or the patient has not recovered from the side effects of such therapy.
16. Patients have received external beam radiation therapy (WBRT, SRS) to the CNS within 21 days of the first dose of the study drug.
17. Patients do not meet prior and concomitant medication criteria (Section 5.5.3).
18. Patients have previously received a BTK inhibitor. Patients who have previously received a BTK inhibitor, but discontinued therapy for reasons other than disease progression are eligible.
19. Patients require > 8 mg/day of dexamethasone or the equivalent.
20. Patients underwent major systemic surgery within <= 2 weeks prior to

enrolling in the study, or who has not recovered from the side effects of such surgery, or who plans to have surgery within 2 weeks of the first dose of the study drug.
21. Patients have undergone prior allogeneic stem cell transplant (autologous stem cell transplant is NOT an exclusion).
22. CAR-T (chimeric antigen receptor T cell) therapy within 60 days of the first dose of GB5121 or ongoing immunosuppressive therapy post CAR-T therapy at the time of screening, clinically significant graftversus-host disease (GVHD), or need for anticytokine therapy for toxicity from CAR-T therapy; residual symptoms of neurotoxicity > Grade 1 from CAR-T therapy.
23. Received a live vaccine within 30 days prior to the first dose of study drug. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist®) are live attenuated vaccines and are not allowed. Approved COVID-19 vaccines are allowed (Emergency Use Authorization and/or full approval).
24. Currently participating in or has participated in a study of an investigational agent or has used an investigational device within 2 weeks prior to the first dose of study drug.

Phase 2: criteria specific to phase 2, the remaining criteria are identical with phase1b
1. Patients with SCNSL or PVRL.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	22
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	GB5121
Generic name:	GB5121

Ethics review

Approved WMO Date:	04-10-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-01-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-03-2023
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	EUCTR2021-006234-39-NL
ClinicalTrials.gov	NCT05242146
CCMO	NL81285.078.22