ISRCTN17975931 https://doi.org/10.1186/ISRCTN17975931

A study to evaluate the safety, tolerability, processing by the body, mechanism of action, and effectiveness of glofitamab following obinutuzumab pretreatment in patients with B-cell non-Hodgkin lymphoma

Submission date 19/06/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 09/08/2021	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 19/08/2025	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Bcell non-Hodgkin lymphoma (NHL) is a type of cancer where white blood cells called B cells grow abnormally and form tumors throughout the body. The aim of this study is to test the drug glofitamab at different doses to establish the safety and effectiveness of subcutaneous (SC) administration of the drug. SC administration is an injection under the skin of the abdomen in a matter of seconds. Glofitamab has been studied previously as an intravenous (IV) infusion. An IV infusion is a slow injection over several hours into a vein in the arm.

Who can participate?

Patients aged over 18 years living with relapsed or refractory Bcell nonHodgkin lymphoma. Relapsed means the cancer has reappeared after a period of remission. Refractory is when the lymphoma does not respond to treatment or when the response to treatment does not last very long.

What does the study involve?

In this study, two drugs will be administered: a pretreatment called obinutuzumab and glofitamab. The pretreatment drug, obinutuzumab, will be administered before the first dose of glofitamab. Obinutuzumab is an antibody that targets the same normal and cancerous cells as glofitamab. Antibodies are a type of blood protein normally made by the immune system to help defend the body against infection and cancer. Obinutuzumab is designed to bind to a protein called CD20 that is present on cancerous B cells, leading to the death of these types of cancer cells. Obinutuzumab has been approved in the United States and Europe for the treatment of B-cell cancers. Obinutuzumab pretreatment will be given as a safety measure to reduce the number of normal and cancerous B cells, mainly in the circulating blood. The reduction of circulating normal and cancerous B cells in advance of receiving the first dose of glofitamab is predicted to reduce any possible side effects that may occur after the first dose of glofitamab.

Glofitamab is a new T-cell bispecific antibody with two arms. One arm recognizes a specific protein called CD20 on the surface of B cells, such as cancerous NHL cells. The other arm recognizes T cells, a type of white blood cell that is critical in the body's immune system. By bringing T cells near the cancerous B cells, glofitamab is designed to activate T cells so they can identify and destroy cancer cells. Glofitamab is an experimental drug, which means health authorities have not approved glofitamab in combination with obinutuzumab for the treatment of NHL.

What are the possible benefits and risks of participating?
All patients will be treated with high-quality technical advanced assessments designed by a group of leading experts in the field of cancer therapy. Participant's health may or may not improve in this study, but the information that is learned may help other people who have a similar medical condition in the future. Participants may have side effects from the drugs or procedures used in this study. Side effects can be mild to severe and even life-threatening, and they can vary from person to person. Participants should talk to the study doctor right away if they have any of the following during the study:
1. Symptoms that are new or have worsened
2. Changes in prescribed or over-the-counter medications (including herbal therapies)
3. Visits to the doctor or hospital, including urgent care or emergency room visits
There may be a risk in exposing an unborn child to study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to study drug. Patients who are pregnant, become pregnant, or are currently breastfeeding cannot take part in this study.

Where is the study run from?
Genentech, Inc (USA)

When is the study starting and how long is it expected to run for?
February 2021 to November 2026

Who is funding the study?
Genentech, Inc (USA)

Who is the main contact?
global-roche-genentech-trials@gene.com

Contact information

Type(s)
Public

Contact name
Mr Clinical Trials

Contact details
1 DNA Way
South San Francisco
United States of America
94080
+1 (0)888 662 6728
global-roche-genentech-trials@gene.com

Additional identifiers

Clinical Trials Information System (CTIS)
2021-000064-29

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
BP43015

Study information

Scientific Title
A Phase Ib, open-label, dose-escalation, multicenter study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of subcutaneous glofitamab following obinutuzumab pretreatment in patients with relapsed or refractory B-cell non-Hodgkin lymphoma

Study objectives
To evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of single-agent glofitamab subcutaneous (SC) in patients with relapsed or refractory B-cell non-Hodgkin lymphoma (R/R NHL).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Australia: Approved 21/05/2021, South Eastern Sydney Local Health District Human Research Ethics Committee (The Sutherland Hospital, Kingsway & Kareena Rd, Caringbah NSW 2229, Australia; +61 (0)2 9540 7756; seslhd-mail@health.nsw.gov.au), ref: 2021/STE00744
2. Belgium: Approved 17/05/2021, Commissie voor medische Ethiek- U/UZ-Gent (Universitair Ziekenhuis Gent, C. Heymanslaan 10 \ B 9000 Gent, Belgium; +32 (0)9 332 41 81; ethisch. comite@uzaent.be), ref: BC-09987
3. Denmark: Approved 24/06/2021, Center for Regional Udvikling De Videnskabsetiske komitéer (De Videnskabsetiske komitéer, Blegdamsvej 60, 1. sal, Opgang 94A11, 2100 København Ø, Denmark; +45 (0)3866 6395; regionh@regionh.dk), ref: H-21026160
4. Italy: Approved 17/06/2021, Comitato Etico di Bergamo (ASST- Papa Giovanni XXIII, P.zza OMS, 1- 24127 Bergamo, Italy; +39 (0)352673341; comitatoetico@asst-pg23.it), ref: 110/21
5. Spain: Approved 14/04/2021, Generalitat Valenciana, Department Clinic Malva-Rosa, Comité De Etica (Avenida Menéndez Pelayo, 4 acc, Tercera Planta, 46010 Valencia, Spain; +34 (0)96 197 39 76; ceic_hcv@gva.es), ref: 2021-000064-29

Study design
Open-label multicenter interventional non-randomized study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
B-cell non-Hodgkin lymphoma

Interventions
All participants will receive pretreatment with a fixed dose of obinutuzumab (Gpt) on Day 1 of Cycle 1 as a safety measure to deplete B cells both in the peripheral blood and in the secondary lymphoid organs, thereby reducing the risk of sudden cytokine release associated with the first glofitamab administration. All participants will receive dexamethasone 20-mg intravenous (IV) prior to each glofitamab dose. Premedication with dexamethasone will be optional for participants with no CRS related to glofitamab in at least two previous cycles based on the investigator's assessment.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Glofitamab (RO7082859), tocilizumab (RO4877533), obinutuzumab (RO5072759), dexamethasone (RO0042867)

Primary outcome(s)
Measured using Electronic Data Capture (EDC):
1. Incidence and severity of CRS following glofitamab SC administration, with severity determined according to American Society for Transplantation and Cellular Therapy (ASTCT) criteria by grade and treatment cycle, up to approximately 44 weeks
2. Incidence and severity of adverse events, with severity determined according to National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0 (NCI CTCAE v5.0), up to approximately 44 weeks
3. Incidence and severity of adverse event of special interest (AESI), up to approximately 44 weeks
4.Targeted vital signs from baseline (up to Day -28) to 44 weeks
5. Targeted clinical laboratory test results from baseline (up to Day -28) to 44 weeks
6. Incidence and severity of dose-limiting toxicities, for Cohort 1: 21 days after the SC dose on Day 15 of Cycle 1; for Cohort 2 and 3: 21 days after the SC dose on Day 1 of Cycle 2
7. Local tolerance at injection sites, including injection-site reactions, up to approximately 44 weeks

Key secondary outcome(s))
Measured using a validated ELISA method:
1. Serum concentration of glofitamab at specified timepoints at Days 1, 8, and 15 of Cycle 1; Day 1 of Cycle 2, 3, 4, 5, 6, 8, 10 and 12; and treatment completion visit
2. Minimum serum concentration under steady-state conditions within a dosing interval/trough concentration (Cmin/Ctrough) of glofitamab, at Days 1, 8, and 15 of Cycle 1; Day 1 of Cycle 2, 3, 4, 5, 6, 8, 10 and 12; and treatment completion visit
3. Delayed time to Cmax (Tmax) of glofitamab at specified timepoints
4. Maximum serum concentration (Cmax) of glofitamab, at Days 1, 8, and 15 of Cycle 1; Day 1 of

Cycle 2, 3, 4, 5, 6, 8, 10 and 12; and treatment completion visit
5. Area under the concentration-time curve (AUC) of glofitamab, at Days 1, 8, and 15 of Cycle 1; Day 1 of Cycle 2, 3, 4, 5, 6, 8, 10 and 12; and treatment completion visit
6. The absolute bioavailability of glofitamab SC administration, at Days 1, 8, and 15 of Cycle 1; Day 1 of Cycle 2, 3, 4, 5, 6, 8, 10 and 12; and treatment completion visit
7. Prevalence of anti-drug antibodies (ADAs) against glofitamab at baseline (up to Day -28)
8. Incidence of ADAs against glofitamab during the study and after treatment completion, at Days 1, 8, and 15 of Cycle 1; Day 1 of Cycle 2, 3, 4, 5, 6, 8, 10 and 12; and treatment completion visit

Completion date
19/11/2026

Eligibility

Key inclusion criteria
1. Participants who are age ≥18 years at the time of signing the Informed Consent Form
2. Participants with a history or status of:
2.1. A histologically confirmed hematological malignancy that is expected to express CD20
2.2. No available treatment options that are expected to prolong survival (e.g., standard chemotherapy or autologous stem cell transplant [SCT])
3. Participants with measurable disease, defined as at least one bi-dimensionally measurable nodal lesion, defined as >1.5 cm in its longest dimension, or at least one bi-dimensionally measurable extra-nodal lesion, defined as >1.0 cm in its longest dimension
4. Participants who are able to provide a fresh biopsy from a safely accessible site, per investigator determination, provided that the participant has more than one measurable target lesion
5. Participants with Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
6. Participants with life expectancy (in the opinion of the investigator) of ≥12 weeks
7. Adverse events from prior anti-cancer therapy must have resolved to Grade 1 or better
8. Participants with adequate liver, hematological and renal function
9. Participants with a negative human immunodeficiency virus (HIV) and hepatitis C virus (HCV) test at screening
10. Participants with a negative serologic or polymerase chain reaction (PCR) test results for acute or chronic hepatitis B virus (HBV) infection
11. For women of childbearing potential: participants who agree to remain abstinent (refrain from heterosexual intercourse) or use contraception during the treatment period and for at least 18 months after the final dose of obinutuzumab, 3 months after the final dose of tocilizumab (if applicable), or 2 months after the final dose of glofitamab, whichever is longer
12. For men: participants who agree to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods, and agree to refrain from donating sperm during the treatment period and for at least 3 months after the final dose of obinutuzumab, tocilizumab (if applicable), or glofitamab, whichever is longer, to avoid exposing the embryo

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Participants who are unable to tolerate subcutaneous injection into the abdomen
2. Participants who are pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after pretreatment with obinutuzumab or 2 months after the final dose of glofitamab, whichever is longer
3. Participants who are unable to comply with protocol-mandated hospitalizations and restrictions
4. Participants with a known or suspected history of hemophagocytic lymphohistiocytosis (HLH)
5. Participants with acute bacterial, viral, or fungal infection at baseline, confirmed by a positive blood culture within 72 hours prior to obinutuzumab pretreatment (Gpt) infusion or by clinical judgment in the absence of a positive blood culture
6. Participants with known active infection, or reactivation of a latent infection, whether bacterial, viral, fungal, mycobacterial, or other pathogens (excluding fungal infections of nail beds) or any major episode of infection requiring hospitalization or treatment with IV antibiotics within 4 weeks of dosing
7. Participants who have had prior treatment with systemic immunotherapeutic agents within 4 weeks or five half-lives of the drug, whichever is shorter, before Gpt infusion on Day 1 of Cycle 1
8. Participants who were previously treated with CD20-CD3 bispecific antibodies (including glofitamab and mosunetuzumab), as this could influence the interpretation of pharmacokinetics and safety
9. Participants with a history of treatment-emergent immune-related adverse events associated with prior immunotherapeutic agents
10. Participants who have been treated with standard radiotherapy, any chemotherapeutic agent, any chimeric antigen receptor-modified T-cell (CAR-T) cell therapy, or any other investigational anti-cancer agent (defined as treatment for which there is currently no regulatory authority approved indication) within 4 weeks prior to Gpt infusion
11. Participants with prior solid organ transplantation
12. Participants with prior allogeneic stem cell transplant (SCT)
13. Participants with autologous SCT within 100 days prior to Gpt infusion
14. Participants with a history of autoimmune disease
15. Participants with a history of severe allergic or anaphylactic reactions to monoclonal antibody therapy or recombinant antibody-related fusion proteins
16. Participants with a history of confirmed progressive multifocal leukoencephalopathy
17. Participants who currently have, or who have a history of, central nervous system (CNS) lymphoma
18. Participants who currently have, or who have a history of, CNS disease such as stroke, epilepsy, CNS vasculitis, or neurodegenerative disease
19. Participants with evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results, including diabetes mellitus, history of relevant pulmonary disorders (bronchospasm, obstructive pulmonary disease) and known autoimmune diseases
20. Participants who have undergone major surgery (excluding biopsies) or significant traumatic injury <28 days prior to the Gpt infusion or who anticipate the need for major surgery during

study treatment
21. Participants who have had another invasive malignancy in the last 2 years
22. Participants who have significant cardiovascular disease such as New York Heart Association Class III or IV cardiac disease, myocardial infarction within the last 6 months, unstable arrhythmias, or unstable angina
23. Participants who have received a live, attenuated vaccine within 4 weeks before Gpt infusion or anticipation that such a live attenuated vaccine will be required during the study
24. Participants who have received systemic immunosuppressive medications within 2 weeks prior to Gpt infusion
25. Participants with a history of illicit drug or alcohol abuse within 12 months prior to screening, in the investigator's judgment
26. Participants with any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that would contraindicate the use of an investigational drug
27. Participants with a history of hypersensitivity to dexamethasone or systemic corticosteroids

Date of first enrolment
03/08/2021

Date of final enrolment
12/12/2025

Locations

Countries of recruitment
Australia

Belgium

Denmark

Italy

Poland

Spain

United States of America

Study participating centre
Prince of Wales Hospital
Haematology
Randwick
Australia
2031

Study participating centre

UZ Gent
C. Heysmanslaan 10
Gent
Belgium
9000

Study participating centre
Rigshospitalet
Hæmatologisk Klinik
Klinisk Afprøvnings Team KAT
Blegdamsvej 9
Afsnit 4032
København Ø
Denmark
2100

Study participating centre
Asst Papa Giovanni XXIII
Ematologia
Piazza OMS-Organizzazione Mondiale della Sanità, 1
Bergamo
Italy
24127

Study participating centre
Istituto Clinico Humanitas
u.O. Oncologia Medica Ed Ematologia
via Manzoni 56
Rozzano
Italy
20089

Study participating centre
Uniwersyteckie Centrum Kliniczne
Osrodek Badan Wczesnych Faz
Smoluchowskiego 17
Gdańsk
Poland
80-214

Study participating centre

Uniwersytecki Szpital Kliniczny
Klinika Hematologii
Nowotworów Krwi i Transplantacji Szpiku
ul. L. Pasteura 4
Wrocław
Poland
50-367

Study participating centre
Szpital Kliniczny im. Przemienienia Panskiego Uniwersytetu Medycznego im. K. Marcinkowskiego w Poznaniu
Oddzial Hematologii i Transplantacji Szpiku
Augustyna Szamarzewskiego 84
Poznan
Poland
60-569

Study participating centre
University of Alabama at Birmingham
354 A Learning Resource Center, 1714 9 th
Birmingham
United States of America
35294

Study participating centre
Icahn School of Medicine at Mount Sinai
One Gustave L. Levy Place
Box 1079
New York
United States of America
10029

Study participating centre
Rutgers Cancer Institute of New Jersey
195 Little Albany Street
New Brunswick
United States of America
08901

Study participating centre

Hospital Universitario Fundación Jiménez Díaz
Oncology & Hematology
Madrid
Spain
28040

Study participating centre
Institut Català d'Oncologia-Hospital Germans Trias i Pujol
Clinical Hematology
Barcelona
Spain
08916

Study participating centre
Hospital Clinic de Barcelona
Department o Hematology
Barcelona
Spain
08036

Study participating centre
Hospital Clinico Valencia
Hematology
Valencia
Spain
46010

Sponsor information

Organisation
Genentech, Inc

Funder(s)

Funder type
Industry

Funder Name

Genentech

Alternative Name(s)
THE GENENTECH FOUNDATION, GF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement for Phase I studies.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes