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A study to assess the safety and distribution of GDC-8264 in combination with standard of care corticosteroid treatment in the blood of participants with high-risk acute graft-versus-host disease (aGVHD)

Submission date	**Recruitment status**	[X] Prospectively registered
07/11/2022	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
09/11/2022	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
04/12/2023	Surgery	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute graft-versus-host disease (aGVHD) is a serious complication that may affect people who have had a bone marrow transplant, a procedure wherein a patient's damaged or diseased blood forming cells (stem cells) are replaced with healthy ones from a different donor. aGVHD occurs when donor cells (called the graft) attack the organs and tissues of the patient who received them (or the host). It can occur any time after transplant and is commonly diagnosed within the first few months. Symptoms usually include skin rashes, stomach or intestinal problems such as nausea, vomiting, or loose stools , and liver damage. Acute GVHD may also increase the risk of developing an infection, which is a major cause of complications (morbidity) and death (mortality) in patients who have undergone a bone marrow transplant.

This study is testing a drug called GDC-8264, which is being developed to treat acute GVHD. GDC-8264 will be given in addition to the standard medications to treat acute GVHD after a bone marrow transplant. GDC-8264 is an experimental drug, which means health authorities have not approved GDC-8264 in combination with standard medications for the treatment of acute GVHD.

The purpose of this study is to evaluate the effects, good or bad, of GDC-8264 plus standard medication on participants who have been diagnosed with acute GVHD and have increased risk of poor clinical response to standard treatment. In this study, the participant will get both GDC-8264 and standard medications [standard of care (SOC)].

Who can participate?
Participants aged 18 years and above with a confirmed diagnosis of aGVHD.

What does the study involve?
Participants will need to be a part of this study for about 1 year. This study will have three parts:

1. A screening visit, where certain tests would be done along with the evaluation of the participant's medical history and ongoing medications to determine if the participant is eligible to take part in the study.

2. Treatment period: eligible participants will receive the study drug (GDC-8264) and the SOC treatment as follows:

SOC medication of either prednisone, given as pills every day, or methylprednisolone, given through the vein [intravenous (IV) infusions] every day. SOC medication will be started up to 3 days before the participant begins receiving GDC-8264. The dose of SOC medication may be increased before starting GDC-8264 and may be reduced (tapered) over time.

GDC-8264, given as pills every day for approximately 28 days. If a participant responds to treatment, GDC-8264 may be continued for another 28 days. Participants may have five or nine visits to the study centre during the treatment period, with each visit lasting about 1-2 hours.

3. A follow-up period during which participants will have check-up visits with the study doctor for a total of 6 times after the treatment completion. Participants will have to visit the clinic or will be contacted via telephone for the follow-up assessments.

What are the possible benefits and risks of participating?
The health of the participant may or may not improve in this study, but the information that is learned may help people with aGVHD 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. The potential side effects of this drug and procedures are listed below.

Risks associated with GDC-8264:
GDC-8264 has had limited testing in humans. Common side effects include headache, dizziness, rash or skin reactions, sleepiness, abdominal pain, loose stools, nausea, and catheter-site bruising. Potential side effects, based on human and animal studies or knowledge of similar drugs, are convulsion and increased risk of bacterial or viral infection.

Risks associated with study procedures:
Blood sampling: Drawing blood can cause pain, bruising, or infection where the needle is inserted. Some participants experience dizziness, fainting, or upset stomach when their blood is drawn.

Mouth Swab: A mouth swab could be painful for a participant if the mouth is inflamed due to acute GVHD. In such cases, the study doctor may wait to take the mouth swab once the inflammation has begun to heal.

There may be a risk in exposing an unborn child to study the drug, and all risks are not known at this time. Women who are pregnant, become pregnant, or are currently breastfeeding, cannot participate 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 2022 to December 2025

Who is funding the study?
F. Hoffmann-La Roche Ltd (USA)

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

Contact information

Type(s)
Public

Contact name
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Additional identifiers

Protocol serial number
GA43861

Study information

Scientific Title
A phase ib, open-label, randomized, dose-finding, multicenter study to evaluate the safety, pharmacokinetics, and efficacy of GDC-8264 in combination with standard of care in the treatment of acute graft-versus-host disease in patients who have undergone allogeneic hematopoietic stem cell transplantation

Study objectives
The primary purpose of the study is to assess the safety and pharmacokinetics (PK) of GDC-8264.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/09/2022, National Marrow Donor Program Institutional Review Board (500 N 5th St Minneapolis, MN 55401, USA; +1(612) 627-5800; IRBstaff@nmdp.org), ref: IRB-2022-0456

Primary study design
Interventional

Study design

Phase Ib open-label randomized dose-finding multicenter study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute graft-versus-host disease

Interventions
GCD-8264, 35 mg: Participants will receive standard-of care (SOC) treatment with prednisone ≥2 milligram per kilogram per day (mg/kg/day), orally (PO), or methylprednisolone ≥2 mg/kg/day, intravenously (IV), for up to 3 days prior to Day 1. Participants will then receive GDC-8264, 35 milligram (mg), PO, once daily (QD) for 28 days. Participants with a clinical response (complete response [CR], very good partial response [VGPR], or partial response [PR]) at Day 28 may also receive GDC-8264 at the same dose level for an additional 28 days, (up to Day 56), at the investigator’s discretion.

GCD-8264, 75 mg: Participants will receive SOC treatment with prednisone ≥2 mg/kg/day, PO, or methylprednisolone ≥2 mg/kg/day, IV, for up to 3 days prior to Day 1. Participants will then receive GDC-8264, 75 mg, PO, QD for 28 days. Participants with a clinical response (CR, VGPR, or PR) may also receive GDC-8264 at the same dose level for an additional 28 days, (up to Day 56), at the investigator's discretion.

Randomization would be done through a central interactive voice or web-based response system (IxRS)

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
GDC-8264

Primary outcome(s)
Measured using patient records:
1. Percentage of Participants with Adverse Events (AEs) and Severity of AEs Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0 Collected from Screening up to End of Study (Up to Approximately 3 years)
2. Plasma Concentration and Relevant PK Parameters of GDC-8264 Measured from Blood Samples Collected at Pre-dose and Multiple Timepoints Post-dose up to Day 57

Key secondary outcome(s)
Measured using patient records:
1. Objective Response Rate (ORR), as Determined by the Investigator From Initiation of Study Treatment to Day 29
2. Duration of Response (DOR), as Determined by the Investigator From Day 29 up to End of Study (Approximately 3 years)
3. Percentage of Participants with Acute Graft-versus-host Disease (aGVHD) Flares, Defined as an Increase in Target Organ Staging For At Least 3 Days Requiring Additional Treatment as

Assessed by Clinical Examination, From Initiation of Study Treatment up to Day 56
4. Percentage of Participants with Non-relapse Mortality (NRM) From Initiation of Study Treatment up to Day 180

Completion date
30/12/2025

Eligibility

Key inclusion criteria
1. Signed Informed Consent Form (ICF) from the participant or legal representative
2. Age ≥18 years at time of signing ICF
3. Diagnosis of post-allogeneic hematopoietic stem cell transplantation (HSCT) aGVHD at screening, with the following aspects of HSCT permissible:
3.1. Any malignant or non-malignant indication leading to HSCT
3.2. Any HSCT donor type (e.g., related, unrelated) or stem cell source (i.e., bone marrow, peripheral blood, cord blood)
3.3. Any GVHD prophylaxis regimen
3.4. Any conditioning regimen (i.e., myeloablative, reduced intensity, and non-myeloablative)
4. Evidence of engraftment post-transplant
5. Diagnosis of high-risk aGVHD, per refined Minnesota high-risk aGVHD criteria during screening
6. Initiation of treatment with systemic corticosteroids for aGVHD at a dose of prednisone ≥2 mg /kg/day PO or methylprednisolone ≥2 mg/kg/day intravenously (or equivalent) in divided doses at diagnosis and up to 3 days prior to or on the same day as initiation of GDC-8264 (Day 1), with no taper planned prior to Day 3

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Evidence of relapsed, progressing, or persistent malignancy, or treatment for relapse after transplant, or requirement for rapid immune suppression withdrawal as pre-emergent treatment of early malignancy relapse
2. Prior receipt of more than one allogeneic HSCT
3. Prior systemic treatment for aGVHD, except for the standard of care corticosteroid treatment initiated as part of this trial
4. Diagnosis of chronic GVHD or overlap syndrome
5. Uncontrolled active infection (i.e., progressive symptoms related to infection despite

treatment, or persistently positive blood cultures despite treatment, or any other evidence of severe sepsis)
6. Severe organ dysfunction (e.g., acute liver failure, renal failure requiring dialysis, ventilator support, or vasopressor therapy)
7. Initiation or planned use of a marketed small molecule (excluding corticosteroids) or biologic therapy as treatment for aGVHD from the start of screening through the treatment period

Date of first enrolment
20/12/2022

Date of final enrolment
30/12/2024

Locations

Countries of recruitment
United States of America

Study participating centre
Icahn School of Medicine at Mount Sinai
United States of America
10029

Study participating centre
Massachusetts General Hospital
United States of America
02114

Study participating centre
Mayo Clinic
United States of America
55905

Study participating centre
Emory University
United States of America
30322

Study participating centre

City of Hope National Medical Center
United States of America
91010

Study participating centre
University of Kansas Medical Center
United States of America
66205

Study participating centre
Columbia University
United States of America
10032

Study participating centre
Vanderbilt Ingram Cancer Center
United States of America
37232

Study participating centre
University of Pennsylvania
United States of America
19104

Study participating centre
Ohio State University
United States of America
43210

Sponsor information

Organisation
Genentech, Inc.

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche Ltd

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.

IPD sharing plan summary
Not expected to be made available

Study outputs

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