ForPatients
by Roche

Acute Graft Versus Host Disease

A Study to Assess the Safety and Pharmacokinetics of GDC-8264 in Combination With Standard of Care in Participants With Acute Graft-Versus-Host Disease (aGVHD)

Trial Status	Trial Runs In	Trial Identifier
Completed	1 Country	NCT05673876 ISRCTN27200385 GA43861

The clinical trial information herein is sourced from public registries such as ClinicalTrials.gov, EuClinicalTrials.eu, and ISRCTN.com. Additional patient-friendly (lay) content has been prepared by Roche to support understanding.

Official 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

Trial Summary:

The primary purpose of the study is to assess the safety and pharmacokinetics (PK) of GDC-8264 in participants with acute graft-versus-host disease (aGVHD).

Genentech, Inc.
Sponsor

Phase 1
Phase

NCT05673876 ISRCTN27200385 GA43861
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

Background and study aim:

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

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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

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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.

Inclusion Criteria:

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- Diagnosis of post-allogeneic hematopoietic stem cell transplantation (HSCT) aGVHD at screening
- Evidence of engraftment post-transplant
- Diagnosis of high-risk aGVHD, per refined Minnesota high-risk aGVHD criteria during screening
- Initiation of treatment with systemic corticosteroids for aGVHD at a dose of prednisone #2 milligrams per kilograms per day (mg/kg/day) by orally (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

Exclusion Criteria:

- 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
- Prior receipt of more than one allogeneic HSCT
- Prior receipt of solid organ transplantation that are target organs for aGVHD (e.g., liver transplant)
- Prior systemic treatment for aGVHD, except for the standard of care corticosteroid treatment initiated as part of this trial
- Diagnosis of chronic GVHD or overlap syndrome
- 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)
- Severe organ dysfunction (e.g., acute liver failure, renal failure requiring dialysis, ventilator support, or vasopressor therapy)
- 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

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