ForPatients
by Roche

Non Hodgkin Lymphoma (NHL)Lymphoma

A clinical trial to look at whether RO7227166 combined with another treatment (either obinutuzumab or glofitamab) is safe and effective at different doses for patients with relapsed or refractory B-cell non-Hodgkin's lymphoma

A Study to Evaluate the Safety, Pharmacokinetics and Preliminary Anti-Tumor Activity of Englumafusp Alfa in Combination With Obinutuzumab and in Combination With Glofitamab Following a Pre-Treatment Dose of Obinutuzumab in Participants With Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	12 Countries	NCT04077723 2019-000416-28 2022-502616-37-00 BP41072

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

An Open-Label, Phase I/II Study to Evaluate the Safety, Pharmacokinetics and Preliminary Anti-Tumor Activity of Englumafusp Alfa (RO7227166, A CD19 Targeted 4-1BB Ligand) in Combination With Obinutuzumab and in Combination With Glofitamab Following a Pre-treatment Dose of Obinutuzumab Administered in Participants With Relapsed/Refractory B-Cell Non-Hodgkin's Lymphoma

Trial Summary:

This is a phase I/II, open-label, dose-escalation study designed to evaluate the safety, tolerability, and efficacy of englumafusp alfa (RO7227166) in participants with relapsed/ refractory Non-Hodgkin's Lymphoma (r/r NHL). Englumafusp alfa will be administered by intravenous (IV) infusion in combination with obinutuzumab and in combination with glofitamab. A fixed dose of obinutuzumab (Gpt; pre-treatment) will be administered up to seven days prior to the first administration of englumafusp alfa and seven days prior to the first administration of glofitamab. This entry-into-human study is divided into a dose-escalation stage (Part I and Part II) and a dose expansion stage (Part III).

Hoffmann-La Roche	**Phase 1/Phase 2**
Sponsor	Phase

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Trial Identifiers

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Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

How does the BP41072 clinical trial work?

This clinical trial is recruiting people who have a type of disease called B-cell non-Hodgkin's lymphoma. In order to take part, patients must have disease that has returned after successful treatment (relapsed) or that has never responded to treatment (refractory).

The purpose of this clinical trial is to test whether RO7227166 combined with either obinutuzumab or glofitamab is safe at different doses, and to look at its effects (good or bad) on you and your non-Hodgkin's lymphoma.

How do I take part in this clinical trial?

To be able to take part in this clinical trial, you must be at least 18 years old and have been diagnosed with relapsed or refractory non-Hodgkin's lymphoma according to specific criteria. The clinical trial doctors will also confirm that there are no other suitable treatment options for you before you take part.

You must not be pregnant, breastfeeding or intending to become pregnant during the clinical trial. If you have certain other medical conditions or have previously received certain treatments, you may not be able to take part in this clinical trial.

If you think this clinical trial may be suitable for you and would like to take part, please talk to your doctor. If your doctor thinks that you might be able to take part in this clinical trial, he/she may refer you to the closest clinical trial doctor. They will give you all the information you need to make your decision about taking part in the clinical trial. You can also find the clinical trial locations on this page.

You will have some further tests to make sure you will be able to take the treatments given in this clinical trial. Some of these tests or procedures may be part of your regular medical care. They may be done even if you do not take part in the clinical trial. If you have had some of the tests recently, they may not need to be done again.

Before starting the clinical trial, you will be told about any risks and benefits of taking part in the trial. You will also be told what other treatments are available so that you may decide if you still want to take part.

While taking part in the clinical trial, both men and women (if you are not currently pregnant but can become pregnant) will need to either not have heterosexual intercourse or take contraceptive medication for safety reasons.

What treatment will I be given if I join this clinical trial?

This clinical trial is made up of three parts: Part I, Part II and Part III. Everyone who joins this study will be given a pre-treatment dose of obinutuzumab before they have any other treatment. This dose of obinutuzumab will be given as an infusion into the vein, either in one day (over 4–5 hours) or split over two days, depending on local guidelines.

If you join Part I of the clinical trial, you will be given:

- RO7227166 as an infusion into the vein roughly seven days after your pre-treatment dose of obinutuzumab, followed by RO7227166 and obinutuzumab as infusions into the vein every three weeks for up to a maximum of two years.

If you join Part II or III of the clinical trial, you will be given:

- Obinutuzumab as a single or double dose. The single dose will be given either seven days or 3–4 days before your first glofitamab dose. The double dose will be given either as two separate administrations the same day (seven days before your first glofitamab dose) or on two separate days (seven days and one day before your first glofitamab dose).
- Glofitamab as an infusion into the vein on Day 1, Cycle 1. Up to three additional doses of glofitamab will be given after the first dose – this is called step-up dosing. Seven days after your last step-up dose of glofitamab, you will be given the first dose of RO7227166 on its own as an infusion into the vein. The next doses of RO7227166 will be given on the same day as glofitamab, every three weeks for up to a maximum of 18 months.
    - One group in Part III will be given glofitamab alone, every three weeks.

Both you and your clinical trial doctor will know which treatment you are being given. Different doses will be tested in different participants but you will only take part in one group.

In the early stages of your treatment, you will need to stay at the hospital for some time so that the clinical trial doctors can watch you closely for any side effects:

- If you join Part I of the clinical trial, you will need to stay at the hospital for at least 48 hours after you have your first and second doses of RO7227166 i.e. you may need to stay in hospital overnight for roughly five nights in total during the first two treatment cycles.
- If you join Part II or III of the clinical trial, you will need to stay at the hospital for at least 24 hours after your first and second (and in some patients, third) step-up doses of glofitamab. If clinical trial doctors see any side effects, you will need to stay at the hospital for 36 hours after your next dose of glofitamab. You will also need to stay at the hospital for at least 48 hours after you have your first and second dose

of RO7227166 (alone and with glofitamab) i.e. you may need to stay in hospital overnight for roughly seven nights in total during the first two treatment cycles.

How often will I be seen in follow-up appointments and for how long?

You are free to stop the clinical trial treatment at any time. If you choose to take part, your total time in the clinical trial will be up to two years if you are in Part I and up to 18 months if you are in Part II or III.

After being given treatment, you will still be seen regularly by the clinical trial doctor roughly every three months, also with blood tests every four weeks and phone calls every two weeks in the first four months.

During follow-up visits, your clinical trial doctor will check how you have responded to treatment and perform scans to make sure that your cancer has not come back. These visits will stop if your cancer comes back.

If you take part in Part II or III of the clinical trial and you responded well to RO7227166 plus glofitamab, you may be able to restart this treatment if your cancer gets worse while you are being seen in follow-up. To do this, your clinical trial doctor may need to repeat some tests to check the treatment is still right for you.

What happens if I am unable to take part in this clinical trial?

If this clinical trial is not suitable for you, you will not be able to take part. Your doctor will suggest other clinical trials that you may be able to take part in or other treatments that you can be given. You will not lose access to any of your regular care.

For more information about this clinical trial see the **For Expert** tab on the specific ForPatient page or follow this link to ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT04077723

Trial-identifier: NCT04077723

Inclusion Criteria:

- History or status of a histologically-confirmed hematological malignancy that is expected to express CD19 and CD20; relapse after or failure to respond to at least one prior treatment regimen; no available treatment options that are expected to prolong survival (Part I and II); relapsed after or failed to respond to only one prior systemic treatment regimen (Part III)
- Must have at least one measurable target lesion (>/= 1.5 cm) in its largest dimension by computed tomography scan
- Able and willing to provide a fresh biopsy from a safely accessible site, per Investigator's determination, providing the participant has more than one measurable target lesion
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, or </= 2 for some participants in Part III

- Life expectancy of >/= 12 weeks
- Adverse events from prior anti-cancer therapy must have resolved to Grade </= 1
- Adequate liver, hematological, and renal function
- Negative test results for acute or chronic hepatitis B virus infection
- Negative test results for hepatitis C virus and HIV
- The contraception and abstinence requirements are intended to prevent exposure of an embryo to the study treatment. The reliability of sexual abstinence for male and/or female enrollment eligibility needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or post-ovulation methods) and withdrawal are not acceptable methods of preventing drug exposure
- Female participants: A female participant is eligible to participate if she is not pregnant and not breastfeeding, and if at least one of the following applies: women of non-childbearing potential (WONCBP); women of child bearing potential (WOCBP) who agree to remain abstinent or use two highly effective contraceptive methods with a failure rate of <1% per year during the treatment period and for at least 18 months after obinutuzumab or 3.5 months after the last dose of englumafusp alfa, 2 months after last dose of glofitamab, or 3 months after the last dose of tocilizumab, whichever is longer. Examples of contraceptive methods with a failure rate of < 1% per year include bilateral tubal occlusion/ ligation, male sexual partner who is sterilized, established proper use of hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices and copper intrauterine devices. Hormonal contraceptive methods must be supplemented by a barrier method; have a negative pregnancy test (blood) within the 7 days prior to the first study treatment administration
- Male participants: During the treatment period and for at least 3 months after obinutuzumab, or 3.5 months after the last dose of englumafusp alfa, 2 months after the last dose of glofitamab, or 2 months after the last dose of tocilizumab whichever is longer, agreement to: Remain abstinent or use contraceptive measures such as a condom plus an additional contraceptive method that together result in a failure rate of < 1% per year, with a partner who is a women of childbearing potential. With pregnant female partner, remain abstinent or use contraceptive measures such as a condom to avoid exposing the embryo; refrain from donating sperm during this same period

Exclusion Criteria:

- Circulating lymphoma cells, defined by out of range (high) absolute lymphocyte count (ALC) or the presence of abnormal cells in the peripheral blood signifying circulating lymphoma cells (for some participants in Part III, ALC only)
- Participants with acute bacterial, viral, or fungal infection at baseline, confirmed by a positive blood culture within 72 hours prior to obinutuzumab infusion or by clinical judgment in the absence of a positive blood culture
- 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
- Pregnant or breast-feeding or intending to become pregnant during the study
- Prior treatment with systemic immunotherapeutic agents, including, but not limited to, radio-immunoconjugates, antibody-drug conjugates, immune/cytokines or monoclonal antibodies within 4 weeks or five half-lives of the drug, whichever is shorter, before obinutuzumab infusion
- History of treatment-emergent immune-related AEs associated with prior immunotherapeutic agents and auto-immune disease
- Treatment with standard radiotherapy, any chemotherapeutic agent, or treatment with any other investigational or approved anti-cancer agent within 4 weeks or 5 half-lives of the drug, whichever is shorter, prior to obinutuzumab infusion
- Prior solid organ transplantation
- Prior allogeneic stem cell transplant
- Autologous stem cell transplant within 100 days prior to obinutuzumab infusion

- History of severe allergic or anaphylactic reactions to monoclonal antibody therapy and confirmed progressive multifocal leukoencephalopathy
- Current or past history of central nervous system (CNS) lymphoma and CNS disease
- 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 and known autoimmune diseases
- Major surgery or significant traumatic injury < 28 days prior to the Gpt infusion or anticipation of the need for major surgery during study treatment
- Participants with another invasive malignancy in the last 2 years
- Significant cardiovascular disease
- Administration of a live, attenuated vaccine within 4 weeks before Gpt infusion or anticipation that such a live attenuated vaccine will be required during the study
- Received systemic immunosuppressive medications (including but not limited to cyclohosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor agents) within two weeks prior to Gpt, with the exception of corticosteroid treatment <=25 mg/day of prednisone or equivalent, however there must be documentation that the participant was on a stable dose of at least a 2-week duration prior to Gpt infusion. Inhaled and topical steroids are permitted