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A study evaluating the effects of the body on and the safety and effectiveness of mosunetuzumab in patients with relapsed or refractory follicular lymphoma

Submission date
03/12/2021

Recruitment status
No longer recruiting

Registration date
08/12/2021

Overall study status
Completed

Last Edited
04/12/2023

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Follicular lymphoma (FL) is a type of cancer that originates in the white blood cells of the body. It is a slow-growing cancer but most patients either experience disease worsening (relapse) after a temporary improvement in symptoms, that lasted a little over 6 months after completion of the last treatment or develop refractory FL (FL that is resistant to treatment or that progressed less than 6 months after completion of the last treatment) (R/R FL). Mosunetuzumab is a trial drug, which means health authorities have not yet approved mosunetuzumab for the treatment of R/R FL. The aims of this study are:
1. To understand how mosunetuzumab is absorbed, distributed, and eventually removed from the body
2. To understand how safe and tolerable mosunetuzumab is when given by itself
3. To assess how effective mosunetuzumab is when given by itself to treat R/R FL
4. To determine how the immune system responds to mosunetuzumab
5. To assess the health status of patients using questionnaires

Who can participate?
People who are over 18 years of age with FL relapsed or refractory to at least two lines of previous systemic therapy.

What does the study involve?
Participants may be asked to be in the study for 1 day or more than 40 months depending on how their cancer responds to the treatment. This includes:
1. A screening period of up to 28 days before the start of the study where tests will be done to check if the participants are eligible to take part in the study.
2. A treatment period where participants will have to visit the clinic roughly every week for the first month, followed by every 3 weeks for receiving treatment. The duration of a visit may be between 2-10 hours. Treatment will be administered under the guidance of a doctor.
3. A safety follow-up period where participants will have a check-up 28 days after receiving the

last dose of mosunetuzumab.
Mosunetuzumab will be given by inserting a needle into a vein in the participant's body (intravenously; IV) over 4 hours during the first cycle. The infusion time will be reduced to 2 hours if there are no infusion-related side effects. The dose will be gradually increased every week during the first cycle. Each cycle is 21 days. Beyond the first cycle, participants will receive the same dose of mosunetuzumab throughout a cycle for 8 or 17 cycles depending on how the tumour is responding to the study treatment. The treatment may be discontinued earlier if FL worsens, or the participant is unable to tolerate the treatment.
To help prevent side effects from mosunetuzumab participants will receive a pain reliever/fever reducer (acetaminophen), and an anti-allergic (diphenhydramine) before every dose. In addition to these a corticosteroid (dexamethasone or a similar medication) will be given before the first four injections (and maybe more depending on whether participants experience certain side effects).
Participants may be allowed to repeat treatment with mosunetuzumab based on how their tumour responds to initial treatment.

What are the possible benefits and risks of participating?
Participants will not receive any benefit from participating in this study, but the information that is learned may help people with certain cancers in the future.
Participants may have side effects from the drugs or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person.
Mosunetuzumab is designed to trigger the body's immune system to fight cancer. This can cause swelling (inflammation) within the tumour and the normal tissues. Therefore, mosunetuzumab may cause several different kinds of side effects related to inflammation. Mosunetuzumab has had limited testing in humans. The known side effects of this drug, as well as potential side effects based on human and laboratory studies or knowledge of similar drugs, are listed below.

Identified risks
1. Cytokine release syndrome/infusion reaction: this is a very common condition that is caused when the immune system releases some proteins called cytokines during study drug infusion. This could cause symptoms of headache, fevers, chills, shortness of breath, rapid heartbeat, changes in blood pressure, and/or muscle aches in the hours or days following the infusion of mosunetuzumab.
2. Neutropenia: a decrease in the number of neutrophils (a type of white blood cell) is another common side effect. A low white blood cell count increases the risk of infections. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
3. Increased risk for infections such as pneumonia (infection of the lungs) which can be severe or fatal, due to the effect of the drug on the immune system.
4. Tumour flare is caused by the action of mosunetuzumab on the cells of the immune system. It can cause symptoms such as shortness of breath (dyspnoea), decreased oxygen levels (hypoxia), elevated levels of compounds that indicate liver damage (liver enzymes and bilirubin, a compound that is produced by the breakdown of red blood cells]), and inflammation of the intestine. Tumour enlargement could also occur, and this may have side effects such as difficulty breathing, or affect major organs, such as the heart or blood vessels, depending on the location of the tumour.
5. Tumour lysis syndrome: this is a condition caused by the rapid destruction of a large number of tumour cells. It may be mild (resulting in some minor changes in blood tests) to severe (resulting in kidney damage).

Potential risks:
1. Thrombocytopenia (low numbers of platelets, a component of the blood that helps it to clot). A low platelet count increases the risk of bleeding (such as nosebleeds, bruising, stroke, and/or

digestive system bleeding).
2. Hemophagocytic lymphohistiocytosis (a severe uncontrolled inflammatory reaction with signs and symptoms that may be similar to those caused by cytokine-release syndrome)
3. A flare-up of past infections (like hepatitis B virus)
4. Progressive multifocal leukoencephalopathy, a rare viral infection
5. There is a chance that the immune system might develop antibodies to this drug, called anti-drug antibodies. Antibodies are proteins made in the body that respond to a substance that is foreign to the body. If these anti-drug antibodies develop, it may affect the body's ability to respond to mosunetuzumab in the future
6. Effects on the nervous system, with symptoms such as headache, dizziness, confusion, speech disorders, tremor, or seizure
7. Liver damage (elevated liver enzymes)

There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Participants who are pregnant, become pregnant, or are currently breastfeeding, cannot take part in this study

Where is the study run from?
F. Hoffmann-La Roche (Switzerland)

When is the study starting and how long is it expected to run for?
June 2021 to April 2025

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

Who is the main contact?
global.trial_information@roche.com

Study website
https://forpatients.roche.com/en/trials/cancer/non-hodgkins-lymphoma/a-study-evaluating-the-effects-of-the-body-on-and-the-safety-and.html

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
YO43555

Study information

Scientific Title
An open-label, multicenter, Phase I trial evaluating the pharmacokinetics, safety, and efficacy of mosunetuzumab as a single agent in patients with relapsed or refractory follicular lymphoma

Study objectives
The aim of this study is to assess the pharmacokinetics, safety, tolerability, and efficacy of mosunetuzumab as a single agent in Chinese patients who were diagnosed with Grade 1-3a follicular lymphoma and have failed two or more lines of systemic therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/09/2021, Ethics Committee of Fudan University Shanghai Cancer Hospital (No. 270, Dong'an Rd, Xuhui District, Shanghai, China, 200032; +86 (0)21 34778299; andwater@163.com), ref: not available

Study design
Phase I open-label multi-centre single-arm study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Relapsed or refractory follicular lymphoma

Interventions
Participants will be given mosunetuzumab intravenously (IV) in a step-up dosing schedule in 21-day cycles for 8 or 17 cycles depending on tumour response unless objective disease progression is documented or unacceptable toxicity occurs earlier.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I

Drug/device/biological/vaccine name(s)
Mosunetuzumab

Primary outcome measure
1. Serum concentration of mosunetuzumab measured using enzyme-linked immunosorbent assay (ELISA) at multiple timepoints points from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)
2. Area under the curve (AUC) of mosunetuzumab derived from the serum concentration-time profiles from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)
3. Maximum concentration (Cmax) of mosunetuzumab derived from the serum concentration-time profiles from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)
4. Minimum concentration (Cmin) of mosunetuzumab derived from the serum concentration-time profiles from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)
5. Total clearance (CL/F) of mosunetuzumab derived from the serum concentration-time profiles from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)
6. Volume of distribution (Vd) of mosunetuzumab derived from the serum concentration-time profiles from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)
7. Terminal half-life (t1/2) of mosunetuzumab derived from the serum concentration-time profiles from Cycle 1 Day 1 up to ≥90 days after last study drug administration (up to approximately 40 months)

Secondary outcome measures
1. Percentage of participants with adverse events and severity per National Cancer Institute-Common Terminology Criteria for Adverse Events Version 5.0 (NCI-CTCAE V5.0) from screening up to approximately 40 months
2. Percentage of participants with adverse events and severity of cytokine release syndrome (CRS) determined per American Society for Transplantation and Cell Therapy (ASTCT) 2019 Consensus Grading Criteria from screening up to approximately 40 months
3. Change from baseline in targeted vital signs measured using clinical examination at every visit from screening up to approximately 40 months
4. Change from baseline in targeted clinical laboratory test results measured using blood and urine samples at multiple timepoints from screening up to approximately 40 months

5. Percentage of participants with dose interruptions, dose reductions, dose intensity, and treatment discontinuation due to adverse events recorded from screening up to approximately 40 months
6. Overall response rate (ORR) as per Independent Review Committee (IRC) according to the 2014 Lugano Response Criteria for Malignant Lymphoma from screening up to approximately 40 months
7. ORR as per investigator from screening up to approximately 40 months
8. Complete response rate (CRR) as per IRC from screening up to approximately 40 months
9. CRR as per investigator from screening up to approximately 40 months
10. Duration of objective response (DOR) as per IRC from screening up to approximately 40 months
11. DOR as per investigator from screening up to approximately 40 months
12. Duration of complete response (CR) as per IRC from screening up to approximately 40 months
13. Duration of CR as per investigator from screening up to approximately 40 months
14. Progression-free survival (PFS) as per IRC from screening up to approximately 40 months
15. PFS as per investigator from screening up to approximately 40 months
16. Overall survival (OS) from screening up to approximately 40 months
17. Number of participants with anti-drug antibodies (ADAs)) measured using validated assay methods at baseline and after initiation of study treatment, up to approximately 40 months
18. Health Status Utility Score measured using EuroQol 5-Dimension Questionnaire 5-Level Version (EQ-5D-5L) from day 1 up to approximately 40 months

Overall study start date
02/06/2021

Completion date
21/04/2025

Eligibility

Key inclusion criteria
1. Age ≥18 years at the time of signing Informed Consent Form (ICF)
2. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
3. Histologically confirmed Grade 1-3a follicular lymphoma who have relapsed after or failed to respond to at least two prior lines of systemic therapy and must have received prior treatment with an anti-CD20-directed therapy and an alkylating agent
4. Participants must have a measurable disease: at least one bi-dimensionally measurable lesion (greater than 1.5 cm in its largest dimension for nodal lesions, or greater than 1.0 cm in its largest dimension for extranodal lesions)
5. Fluorodeoxyglucose (FDG)-avid lymphoma [i.e., positron emission tomography (PET) - positive lymphoma]
6. Adverse events from prior anti-cancer therapy resolved to ≤ Grade 1 (with exceptions of alopecia and anorexia)
7. Residence in the People’s Republic of China

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
15

Total final enrolment
17

Key exclusion criteria
1. Participants who are pregnant or breastfeeding, or intending to become pregnant during the study or within 3 months after the final dose of mosunetuzumab and 3 months after the last dose of tocilizumab (if applicable)
2. Prior use of any monoclonal antibody, radioimmunoconjugate, or antibody-drug conjugate within 4 weeks before the first mosunetuzumab administration
3. Prior treatment with systemic immunotherapeutic agents for which the mechanism of action involves T cells within 12 weeks or five half-lives of the drug, whichever is shorter, before first Mosunetuzumab administration
4. Treatment-emergent immune-related adverse events associated with prior immunotherapeutic agents (e.g., immune checkpoint inhibitor therapies)
5. Treatment with any chemotherapeutic agent, or treatment with any other anti-cancer agent (investigational or otherwise) within 4 weeks or five half-lives of the drug, whichever is shorter, prior to first mosunetuzumab administration
6. Treatment with radiotherapy within 2 weeks prior to the first mosunetuzumab administration
7. Autologous stem cell transplant (SCT) within 100 days prior to first mosunetuzumab administration
8. Prior treatment with CAR-T therapy within 30 days before first Mosunetuzumab administration
9. Prior allogeneic SCT
10. Prior solid organ transplantation
11. History of autoimmune disease but participants with a remote history of, or well-controlled autoimmune disease may be eligible to enrol
12. Participants with a history of macrophage activation syndrome (MAS)/hemophagocytic lymphohistiocytosis (HLH)
13. Participants with a history of confirmed progressive multifocal leukoencephalopathy (PML)
14. Current or past history of CNS lymphoma
15. Known or suspected chronic active Epstein-Barr Virus infection (CAEBV)

Date of first enrolment
10/12/2021

Date of final enrolment
28/10/2022

Locations

Countries of recruitment
China

Study participating centre
Fujian Provincial Cancer Hospital
China
350014

Study participating centre
Sun Yet-sen University Cancer Center
China
510060

Study participating centre
Fudan University Shanghai Cancer Center
China
200120

Study participating centre
Tianjin Cancer Hospital
China
300060

Study participating centre
Union Hospital Tongji Medical College
Huazhong University of Science and Technology
China
430023

Study participating centre
Henan Cancer Hospital
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450008

Sponsor information

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Roche (Switzerland)

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Sponsor type
Industry

Website
https://www.roche.com/about_roche/roche_worldwide.htm

ROR
https://ror.org/00by1q217

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date

31/12/2024

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