A COMPARATIVE, RANDOMIZED, PARALLEL-GROUP, MULTI-CENTRE, PHASE IIIB STUDY TO INVESTIGATE THE EFFICACY OF SUBCUTANEOUS (SC) RITUXIMAB VERSUS INTRAVENOUS (IV) RITUXIMAB BOTH IN COMBINATION WITH CHOP (R-CHOP) IN PREVIOUSLY UNTREATED PATIENTS WITH CD20 POSITIVE DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL).

Published: 10-07-2012
Last updated: 26-04-2024

The objective of this study is to gather more information to find out if one of these rituximab administration methods is more effective and safer in the treatment of DLBCL patients. This study will also collect information on patient satisfaction...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Interventional

Summary

ID

NL-OMON41547

Source
ToetsingOnline

Brief title
MabEase

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Diffuse Large B-Cell Lymphoma, lymph node cancer

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Roche Nederland B.V.

Intervention

Keyword: Intravenous, Lymphoma, Rituximab, Subcutaneous

Outcome measures

Primary outcome

The primary objective for this study is to estimate the efficacy of rituximab administered subcutaneously (SC) or intravenously (IV) in combination with cyclophosphamide, vincristine, doxorubicin, and prednisone (CHOP), as measured by complete response rate (including complete response unconfirmed; CR/CRu) approximately one month after the end of rituximabbased treatment.

Secondary outcome

• To compare patient satisfaction with rituximab SC versus rituximab IV in patients with diffuse large B-cell lymphoma (DLBCL), as measured by the validated Cancer Treatment Satisfaction Questionnaire (CTSQ) and the Rituximab Administration Satisfaction Questionnaire (RASQ).

• To evaluate the effects of method of administration (rituximab SC or

rituximab IV) in terms of:

- Rituximab administration time, defined as the time from start to end of the rituximab SC injection or from start to end of the rituximab IV infusion

- Chair time defined as the time the patient occupies an infusion chair/bed for a single treatment cycle of R-CHOP immunochemotherapy

- Hospital time, defined as the time the patient is in hospital for the course of one cycle of R-CHOP immunochemotherapy.

• To evaluate event-free survival (EFS), disease-free survival (DFS), progression-free survival (PFS) and overall survival (OS) from randomization.

• To evaluate the safety of rituximab SC compared with rituximab IV in patients with DLBCL, focusing on serious adverse events (SAEs), Grade >= 3 adverse events (AEs), and Grade >= 3 application associated reactions (AAR) and infusion related reactions (IRR)) according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 4.0).

Study description

Background summary

Roche is investigating the subcutaneous injection into the skin of rituximab (referred to as subcutaneous rituximab) compared to the intravenous rituximab administration. Compared to IV administration, the SC injection will only take 5 to 6 minutes. This simple SC injection will allow the time of patient stay to reduce significantly compared to IV administration. This reduction will also apply to hospital burden associated with IV administration. Additionally, Roche expects that the subcutaneous administration will increase patient satisfaction, ease of administration and treatment compliance.

Study objective

The objective of this study is to gather more information to find out if one of

these rituximab administration methods is more effective and safer in the treatment of DLBCL patients. This study will also collect information on patient satisfaction with the rituximab treatment and on the time spent in the hospital during the rituximab treatment.

Study design

This is a Phase IIIb, prospective, multi-centre, multinational, open label randomized study in approximately 600 adult patients with previously untreated CD20-positive DLBCL.

Patients will be randomized to either group A or B in a 2:1 ratio. All patients will receive 8 cycles of rituximab treatment (unless unacceptable side effects occur or the disease does not improve or progresses) in combination with either 6 or 8 cycles of CHOP-21, or 6 or 8 cycles of CHOP-14. Rituximab will be administered on the same day, prior to the CHOP administration, or on the day before CHOP administration, for a total of 8 treatment cycles. Patients receiving rituximab with 6 cycles of CHOP-14 will receive 2 additional cycles consisting of rituximab only, for a total of 8 cycles of rituximab (without CHOP).
Patients in groep A will receive rituximab IV for their first treatment cycle, followed by SC rituximab for the remaining 7 treatment cycles. If patients in group A have a reaction to the first treatment with IV rituximab or are unable to receive the full dose, they will continue to receive IV rituximab for their secont treatment cycle.
Patients in group B will receive rituximab IV for all 8 treatment cycles.

Intervention

Patients eligible for participation in the study will be treated according to the specific study schedule in protocol v3.0, 20 March 2013 (appendix 1, page 98-100).

Study burden and risks

The study procedures and treatments may be associated with risks and may cause discomfort. There is a risk of slight pain or bruising when blood is collected. Bone marrow sampling may give a risk of serious bleeding and/or infection where the sample is taken, but these are rare.
Undergoing MRI or CT scans exposes the patient to low dose of radiation. The dye used in some CT scans and MRIs may cause serious allergic reactions that can be life-threatening without treatment.
There may be side effects associate with rituximab IV; fever and chills, nausea (feeling like you are going to throw up), vomiting (throwing up), fatigue (feeling tired or weak), headache, skin rash, redness of the skin, itchiness, wheezing or tightness in the chest, shortness of breath, difficulty breathing,

sensation of the tongue or throat swelling, throat irritation, rhinitis (runny nose), temporary low blood pressure, flushing, dizziness on standing up, fast heartbeat, chest pain, or pain where the tumour is located. These side effects are usually mild to moderate and can be easily treated. Rarely, these reactions can be severe. These side effects are less common after the first treatment with IV rituximab.
Treatment with rituximab may cause a higher risk for infection due to the way rituximab works to kill blood and tumour cells.
Very common side effects have been seen in at least 1 person for every 10 people receiving rituximab with or without chemotherapy in a research study. These include infections caused by viruses or bacteria; bronchitis; fever; chills; low white blood cell count with or without a fever; low antibodies in the blood (antibodies help fight infection); low blood platelets (platelets help control bleeding); swelling of the face, lips, mouth or throat (this may cause difficulty in swallowing or breathing); nausea; muscle weakness; skin rash; itching; headache; and hair loss.

Common side effects have been seen in at least 1 person for every 100 people receiving rituximab with or without chemotherapy in a cancer research study. These include blood infections; lung and airway infections; fungal infections; shingles (itchy tingling areas, usually on your trunk, that become painful blisters); hepatitis B infection; cold symptoms; changes to the blood (such as changes that lower the bloods ability to provide oxygen to the tissues, fight infection and to prevent bleeding as well lower levels of calcium and higher levels of sugar and cholesterol); widening of the blood vessels; swelling of the hands, feet or ankles; numbness; numbness with a prickly feeling; allergic reactions; hives; skin problems; eye tearing; eye infection; ear pain; ringing in the ears; heart beat abnormalities, heart attack, and other heart problems (these can result in chest pain and noticeable changes to your heart beat); chest pain; high blood pressure; low blood pressure; inflammation, irritation and/or tightness of the lungs; shortness of breath; cough; rhinitis (stuffy nose); sinusitis (stuffy sinuses); mouth inflammation; difficulty swallowing; throat irritation; indigestion; abdominal pain; vomiting; diarrhoea; constipation; loss of appetite; weight loss; fatigue; dizziness; shivering; sweating; trouble sleeping; night sweats; agitation; anxiety; malaise; reddening of the face and body; increased muscle tension; muscle pain; joint pain; back pain; neck pain; and tumour pain.
Uncommon side effects have been seen in at least 1 person for every 1000 people receiving rituximab with or without chemotherapy in a research study. These include: bleeding; depression; nervousness; change to sense of taste; blood clotting problems; swelling of the lymph nodes; asthma; lung problems including inflammation and scarring that narrow the airways; not enough oxygen to the body; abdominal swelling ; and pain at the site where rituximab was given.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age >= 18 and <= 80 years at time of study inclusion ;• Histologically confirmed, previously untreated CD20-positive DLBCL according to the WHO classification system;• Patients with an IPI score of 1-5 or IPI score of 0 with bulky disease, defined as one lesion >= 7.5 cm;• At least one bi-dimensionally measurable lesion defined as >= 1.5 cm in its largest dimension on CT scan, PET-CT scan or MRI;• Adequate hematologic function;• Eastern Cooperative Oncology Group (ECOG) performance status <= 2.

Exclusion criteria

• Primary or secondary central nervous system lymphoma, histologic evidence of transformation to Burkitt lymphoma, primary mediastinal DLBCL, primary effusion lymphoma,

primary cutaneous DLBCL, or primary DLBCL of the testis ;• Transformed lymphoma or follicular lymphoma IIIB ;• Prior therapy for DLBCL, with the exception of nodal biopsy or local irradiation ;• History of other malignancy, except for curatively treated basal or squamous cell carcinoma or melanoma of the skin, carcinoma in situ of the cervix, or a malignancy that has been treated without curative intent and has been in remission without treatment for >= 5 years prior to enrolment ;• Inadequate renal or hepatic function ;• Known human immunodeficiency virus (HIV) infection or HIV seropositive status ;• Active hepatitis B virus (HBV) or active hepatitis C virus (HCV) infection ;• History of severe allergic or anaphylactic reactions to humanized or murine monoclonal antibodies or known sensitivity or allergy to murine products ;• Contraindication to any of the individual components of CHOP, including prior receipt of anthracyclines ;• Prior treatment with cytotoxic drugs or rituximab for another condition (e.g. rheumatoid arthritis) or prior use of an anti-CD20 antibody ;• Pregnant or lactating women

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-01-2013
Enrollment:	42
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	MabThera
Generic name:	rituximab

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MabThera
Generic name:	rituximab / rHuPH20 SC

Ethics review

Approved WMO Date:	10-07-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-09-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-11-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-11-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-04-2013
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-04-2013
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	15-10-2013
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-12-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-000669-19-NL
Other	Het onderzoek is onder het EudraCT nummer terug te vinden op www.rochetrials.com

Register ID

CCMO NL41113.056.12