ISRCTN26918647 https://doi.org/10.1186/ISRCTN26918647

Study of RTXM83 plus CHOP chemotherapy versus a rituximab plus CHOP therapy in patients with Non Hodgkins lymphoma

Submission date
27/09/2012

Recruitment status
No longer recruiting

Registration date
18/07/2013

Overall study status
Completed

Last Edited
01/02/2019

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Non-Hodgkins lymphoma is a type of cancer that affects the network of vessels and glands throughout the body. We are comparing a drug called biosimilar rituximab against rituximab, both given with chemotherapy for patients with non-Hodgkins lymphoma. The main purpose of the study is to prove that the treatment with biosimilar rituximab has similar effects as the treatment with rituximab. Additionally, we will check the time taken for this disease to progress and review the safety of both drugs.

Who can participate?
The study aims to enrol 250 patients, men and women, aged 18 to 65, recently found to have this disease and who have not received any treatment for it before.

What does the study involve?
Patients are randomly allocated to one of two groups: one will be treated with biosmiliar rituximab and the other one with rituximab, both treatments combined with CHOP chemotherapy, on day 1 every 3 weeks for 6 cycles. There will be 3 study periods: screening (various tests will be done including a complete physical examination), treatment (visit the clinic every 3 weeks to undergo 6 cycles of treatment) and a final visit (30 days after completion of the treatment). After this, patients will be followed up every 3 months until 9 months after the last dose of chemotherapy.

What are the possible benefits and risks of participating?
Taking part in this study may or may not make your health better. This study might contribute to the development of a drug that will lower the cost of currently available treatment options. This information may help future patients. Patients may have side effects caused by the drug rituximab. The main ones are due to the drip (infusion of the drug) given during the treatment. These are mainly seen with the first drip and rarely require drug treatment to be stopped. Also, low blood pressure, fever, chills, episodes of shaking/shivering, skin rash, tightening of the airways and swelling of the deeper layers of the skin have been observed with this drug infusion. Possible serious side effects of CHOP chemotherapy include infection, bleeding problems, tissue

injury, early menopause, heart failure and bladder problems. Common side effects of CHOP chemotherapy include nausea and vomiting, fevers and chills, skin rash, hair loss, mouth sores, fatigue, platelets in your blood may decrease (platelets help your blood clot if you cut yourself and you may bruise or bleed more easily than usual), severe constipation, numbness or tingling of fingers or toes, pink or reddish urine for 1-2 days after treatment, sugar control may be affected in people with diabetes, increased energy and difficulty sleeping.

Where is the study run from?
The study is run at different hospitals and clinics in Argentina, Brazil, Mexico, Venezuela, Paraguay, Indonesia, India, Colombia and South Africa.

When is the study starting and how long is it expected to run for?
The study started in January 2013 in Paraguay, April 2013 in Argentina, May 2013 in Indonesia and Mexico. It is expected that study will start in August 2013 in Brazil and South Africa and at the end of the year in Venezuela, India and Colombia. The study will be recruiting patients until December 2014.

Who is funding the study?
The present study is sponsored by mAbxience SA (Switzerland) and co-sponsors as this is a co-development study.

Who is the main contact?
Mrs Susana Millán,
Susana.Millan@chemogroup.net (English/Spanish)

Contact information

Type(s)
Scientific

Contact name
Mrs Susana Millan

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Quintanapalla N2
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Additional identifiers

Protocol serial number
RTXM83-AC-01-11

Study information

Scientific Title
A randomized, double-blind, phase III study comparing biosimilar rituximab (RTXM83) plus CHOP chemotherapy versus a reference rituximab plus CHOP (R-CHOP) in patients with Diffuse Large B-Cell Lymphoma (DLBCL) given as first line

Study objectives

The primary endpoint of the investigation is to determine if the response rate obtained with RXM83 combined with CHOP is non inferior to the response rate obtained with reference rituximab combined with CHOP
The present study is a non inferiority trial and the study hypothesis is the following: H0: pc ≥ pe + δ vs. H1: pc < pe + δ where,
pe: proportion of successes in the experimental group (RTXM83+CHOP)
pc: proportion of successes in the control group (Reference Rituximab+CHOP)
Type I error: the difference pc-pe is less than δ when in fact the difference is greater than or equal to δ ie, we choose the experimental treatment when the control treatment is actually substantially better.
Type II error: the difference -pe is greater than or equal to δ when it is actually lest than δ ie, we choose the control treatment when the experimental treatment is essentially just as good.

Ethics approval required

Old ethics approval format

Ethics approval(s)

7-May-2012 Ref No. NAP Comité Independiente de Ética para Ensayos en Farmacología Clínica (FEFYM), Buenos Aires, Argentina
31-May-2012 Ref No. NAP Consejo de Bioética. Sistema Provincial de Salud. Ministerio de Salud Pública de la Provincia de Tucumán, Argentina
19-Jul-2012 Ref No. HP-422 Comité Institucional de Ética de Investigación en Salud Hospital Privado-Centro Médico de Córdoba
24-Oct-2012 Ref No. 773/2012 Comité de Ética de Investigación Facultad de Ciencias Médicas Universidad Nacional de Asunción, Asunción, Paraguay
23-Jul-2012 Ref No. 059/PEP/07/2012 The Committee of the Medical Research Ethics of the Dharmais Cancer Hospital
24-Jul-2012 - Ref No. 62340 - Ethic Committee of Faculdade de Ciencias Medicas UNICAMP - Centro de Hematologia e Hemoterapia - HEMOCENTRO
10-Sep-2012 Ref No. NAP Gobierno de la Ciudad de Buenos Aires Comité de Ética en Investigación Hospital General de Agudos Donación Francisco Santojanni
13-Sep-2012 Ref No. NAP Comité de Ética Hospital Nacional de Clínicas Universidad Nacional de Córdoba
02-Oct-2012 - Ref No. NAP Comité de Ética del Centro Clínico San Cristóbal Hospital Privado, C. A., San Cristóbal, Táchira, Venezuela
05-Oct-2012 Ref No. NAP Comité de Revisión Institucional del Hospital Británico
05-Oct-2012-Ref No. NAP Comité de Ética de la Clínica Dr. A.L. Briceño Rossi, Caracas, Distrito Capital, Venezuela
07-Dec-2012 Ref No. NAP Comité Institucional de Ética Sanatorio Allende, Córdoba, Argentina
20-Dec-2012 Ref No. NAP Comité de Ética en Investigación Universidad de Buenos Aires Instituto de Oncología Ángel H. Roffo12-Feb-2013 Ref No. 121111 University of the Witwatersrand, Human Research Ethics Committee (HREC) and the Protocol Review Committee (PRC), Johannesburg, South Africa
16-Feb-2013 Ref No. 194.564 - Comissão Nacional de Ética em Pesquisa, Brasilia, Brazil

Study design

Prospective phase III multicenter double-blind randomized study

Primary study design

Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diffuse large b-cell lymphoma (DLBCL)

Interventions
RTXM83 and Rituximab will be administered as : 375 mg/m2 I.V., every 3 weeks on Day 1 of the CHOP regimen, with a total of 6 cycles.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Response Rate

Key secondary outcome(s))
1. To evaluate Event Free Survival (EFS) in both treatment arms
2. To evaluate Safety in both arms
3. To demonstrate comparable pharmacokinetics of RTXM83 and Rituximab
4. To demonstrate comparable pharmacodynamics
5. To compare immunogenicity between both arms

Completion date
30/05/2014

Eligibility

Key inclusion criteria
1. Patients with measurable disease defined as existence of a unidimensional or bidimensional lesion greater than 2 cm in its longest diameter or malignant lymphocytosis greater than 5x109 /L. Any other procedure for measurable disease in particular cases, may be allowed upon Sponsor approval
2. Newly diagnosed patients with a confirmed pathologic diagnosis of large B cell-non-Hodgkins lymphoma (DLBCL) with untreated CD20+. Defined by the local Haematopathologist at the local laboratory according to WHO criteria
3. Stage II-III or IV or stage I with bulk defined by the referring physician on the basis of the Cotswolds modification of the Ann Arbor classification 2
4. Age-adjusted International Prognostic Index (IPI) score 0 or 1
5. Age ≥18 to ≤65 years of age
6. Performance status (Eastern Cooperative Oncology Group [ECOG]) of ≤2
7. Written informed consent obtained before starting any study-specific procedure

8. Females of child-bearing potential must test negative on standard serum pregnancy test and must be willing to practice appropriate contraceptive methods for the duration of the study (e.g. oral contraceptive, double barrier method, intra-uterine device, intra-muscular contraceptive)
9. All male patients must take adequate contraceptive precautions during the course of the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Life expectancy of less than three months
2. Any other lymphoma other than CD20+ DLBCL
3. Indolent lymphoma, Primary central nervous system (CNS) Lymphoma or gastro-intestinal Mucosa Associated Lymphoid Tissue (MALT) Lymphoma
4. Known hypersensitivity to active ingredients, excipients and murine and foreign proteins
5. Concurrent disease or general status that would exclude giving the treatment as outlined in the protocol
6. Active uncontrolled infection requiring systemic treatment with antibiotics or antiviral agents at Screening or history of documented recurrent clinically significant infection (e.g. 2 or more viral, bacterial or fungal infections requiring inpatient treatment)
7. Cardiac contra-indication to Doxorubicin therapy: non-compensated heart failure, dilated cardiomyopathy, coronary heart disease with ST segment depression on electrocardiogram (ECG), myocardial infarction in the last 6 months
8. Neurologic contra-indication to Vincristine as it is indicated in the SmPC: (e.g. peripheral neuropathy)
9. Chronic lung disease with hypoxemia measured by saturometer (gasometry is not mandatory)
10. Severe uncontrolled hypertension, despite optimal medical treatment
11. Severe uncontrolled diabetes mellitus, despite optimal medical treatment
12. Renal insufficiency (Serum Creatinine>2xUNL)
13. Hepatic insufficiency (aspartate aminotransferase [AST]/alanine aminotransferase [ALT] >3xUNL or >5xUNL with involvement of the liver, total bilirubin >34.2 µmol/L, or both) not related to lymphoma
14. Clinical signs of cerebral dysfunction
15. Severe psychiatric disease
16. Known human immunodeficiency virus (HIV) infection or active chronic hepatitis B or C
17. Abnormal bone marrow function (platelets <100x109/L, neutrophils <1.5x109/L and Haemoglobin <9g/dL)
18. Post-transplantation lymphoproliferative disease
19. Pregnant or lactating women or women that intend to get pregnant during study or within 12 months following the last infusion

20. Treatment with any investigational product in the 30 days period before inclusion in the study
21. Prior radiotherapy to treat the DLBCL NHL
22. Limitation of the patients ability to comply with the treatment or follow-up protocol

Date of first enrolment
30/11/2012

Date of final enrolment
30/05/2014

Locations

Countries of recruitment
Argentina

Brazil

Colombia

India

Indonesia

Mexico

Paraguay

South Africa

Spain

Venezuela

Study participating centre
Quintanapalla N2
Madrid
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28050

Sponsor information

Organisation
mAbxience (Switzerland)

Funder(s)

Funder type
Industry

Funder Name
A partnership has been established between mAbxience SA (Switzerland) and other pharmaceutical companies for the development of this large, phase III, multicentre clinical trial with this product, each company contributing to support the complete cost of the trial

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration