ISRCTN05147495 https://doi.org/10.1186/ISRCTN05147495

Rational use of substrate reduction therapy and enzyme replacement therapy in patients with type I Gaucher disease (Uso racional de los tratamientos por inhibición de sustrato y enzimático sustitutivo en pacientes con enfermedad de Gaucher tipo I)

Submission date
31/01/2011

Recruitment status
No longer recruiting

Registration date
18/04/2011

Overall study status
Completed

Last Edited
18/04/2011

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Pilar Giraldo Castellano

Contact details
Servicio de Hematología
Hospital Universitario Miguel Servet
Paseo Isabel La Católica 1-3
Zaragoza
Spain
50009
+34 670285339
giraldo.p@gmail.com

Additional identifiers

Protocol serial number

EC-90737

Study information

Scientific Title
Rational use of substrate reduction therapy and enzyme replacement therapy in patients with type I Gaucher disease: an open-label single-centre follow up study

Study objectives
The aim of this study is to evaluate the long-term effect of miglustat (substrate reduction therapy) as first-line treatment in mild to moderate Gaucher Disease (GD) and its effectiveness as maintenance therapy either in patients with type I GD who have achieved a stable condition with enzyme replacement therapy or in patients with severe disease who have not reached the objectives of the treatment.

Substrate Reduction Therapy (SRT) is an effective alternative to Enzyme Replacement Therapy (ERT) in type I GD. It is administered orally, therefore it is more comfortable, has lower direct and indirect administration costs. The SRT would have indication and efficacy in patients who have reached treatment goals, for who maintaining response is necessary and in patients with advanced disease who have not reached treatment goals.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Clinical Research Ethics Committee of Aragon (Comité Ético de Investigación Clínica de Aragón (CEICA).
Ref: C.I. EC07/083, 20/05/2008

Study design
Open-label single centre follow-up study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type I Gauchers disease

Interventions
Asymptomatic patients with a severity scale of 0-3 points are not treated but monitored and assessed every 6 months (clinically, laboratory and imaging). New diagnosed symptomatic patients with a severity scale of 0-3 points would be eligible for SRT (100 mg/TID PO) or ERT (30 U/kg IV every 2 weeks) in function of individual characteristics and preferences. New diagnosed symptomatic patients with a severity scale of 4-8 points would be eligible for SRT (100 mg/TID PO) or ERT (60 U/kg IV every 2 weeks) in function of individual characteristics and preferences. New diagnosed symptomatic patients with a severity scale >9 points will receive ERT (60 U/kg IV every 2 weeks). Patients previously treated with ERT and have reached stability for a minimum

of 2 years will receive treatment with SRT (100 mg/TID PO). For all treatment arms, the patients will be followed during 24 months. Test that will be run: Magnetic resonance imaging (MRI) spleen and liver volume measurement (basal and every 6 months), MRI femoral and lumbar spinal bone marrow infiltration (basal and months 12 and 24), biomarkers of GD activity such as chitotriosidase, angiotensin-converting enzyme (ACE), tartrate-resistant acid phosphatase (TRAP) and ferritin, and including platelets, hemoglobin and vit B12 (all visits), QLQ SF-36 (basal and months 12 and 24), global improvement scale (patient / investigator, all visits from visit 2), Visual Analog Scale for pain assessment (all visits), neurologic and neuropsychological tests including electroneurography (basal and every 6 months), physical examination and vital signs (basal and months 12 and 24)

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
The primary end point is the percentage change in liver volume in baseline visit and every six months upto 24 months measured by MRI

Key secondary outcome(s))
1. The percentage change in spleen volume every six months and bone marrow infiltration measured yearly [baseline visit (visit 1), 12 months (visit 4) and 24 months (visit 6)] by MRI 2. Changes in hAematologic parameters (haemoglobin, platelets)
3. Chitotriosidase activity measured every two years (in baseline visit and visit 6)

Completion date
31/12/2011

Eligibility

Key inclusion criteria
1. Patients ≥ 18 years. Diagnosis of type I GD confirmed by glucocerebrosidase assay or by the presence of mutations in the glucocerebrosidase gene
2. Patients who have received enzyme replacement therapy for at least 3 years with the same dose for at least the last 6 months
3. Stable clinical and biological disease for 2 years confirmed with at least two assessments including the one performed at baseline

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. History of oculomotor palsy, ataxia or other manifestations usually associated with type 3 GD
2. Splenectomy before 18 years due to massive splenomegaly or severe cytopenia
3. Documented peripheral polyneuropathy. Intolerance to lactose
4. Diarrhoea of unknown origin within 6 months prior to visit 1 or history of significant gastrointestinal disorders
5. Cataracts or a known risk of cataract formation
6. Severe renal insufficiency
7. Active intercurrent diseases, such as human immunodeficiency virus (HIV) or hepatitis B or C
8. Dependence or current abuse of drugs or alcohol
9. Suspected hypersensitivity to miglustat or any of the excipients
10. Patients who have previously received miglustat
11. Pregnancy or breast-feeding
12. Patients who refuse to use a reliable contraceptive method throughout the study and during the three months following the discontinuation of miglustat
13. Patients receiving treatment with another investigational product or have received an investigational product in the 3 months prior to baseline

Date of first enrolment
01/12/2009

Date of final enrolment
31/12/2011

Locations

Countries of recruitment
Spain

Study participating centre
Servicio de Hematología
Zaragoza
Spain
50009

Sponsor information

Organisation

Aragon Institute of Health Sciences [Instituto Aragonés de Ciencias de la Salud] (Spain)

ROR
https://ror.org/05p0enq35

Funder(s)

Funder type
Government

Funder Name
Aragon Institute of Health Sciences [Instituto Aragonés de Ciencias de la Salud] (Spain)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration