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A randomised, multicentre, open label, phase II study to evaluate the safety, tolerability, pharmacokinetics and the effects on liver iron concentration of repeated doses of 10 mg/kg /day of ICL670 relative to deferoxamine in sickle cell disease (SCD) patients with transfusional haemosiderosis

Submission date
23/07/2003

Registration date
05/09/2003

Last Edited
21/03/2016

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Haematological Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Elliot Vichinsky

Contact details
Children's Hospital & Research Center at Oakland
747 52nd Street
OPC-PCRC, 1st Floor
Oakland
United States of America
94609-1809

Additional identifiers

EudraCT/CTIS number

2004-000597-31

IRAS number

ClinicalTrials.gov number
NCT01090323

Secondary identifying numbers
CICL670 0109

Study information

Scientific Title
A randomised, multicentre, open label, phase Il study to evaluate the safety, tolerability, pharmacokinetics and the effects on liver iron concentration of repeated doses of 10 mg/kg/day of ICL670 relative to deferoxamine in sickle cell disease (SCD) patients with transfusional haemosiderosis

Acronym
ICL109

Study objectives
The primary objective of this randomised, open-label, phase II trial was to evaluate the safety and tolerability of deferasirox in comparison with deferoxamine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The trial was conducted in accordance with the Declaration of Helsinki. Institutional Review Board approval was obtained at each participating institution and written informed consent was obtained from all patients or guardians prior to participation in any study procedures.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Sickle cell disease (SCD)

Interventions
The study duration was 52 weeks. The initial 24 patients enroled were randomised to receive deferasirox 10 mg/kg or deferoxamine at recommended doses of 20 - 60 mg/kg based on initial liver iron concentration (LIC).

Subsequently, additional safety information became available for deferasirox suggesting a need to modify the starting dose. Therefore, following the enrolment of the first 24 patients, the study was amended so that all subsequent patients randomised to deferasirox were dosed at 10 - 30 mg/kg according to baseline LIC.

Deferasirox was given once daily each morning as a dispersed solution in water, half-an-hour before breakfast.

Deferoxamine was administered as a slow subcutaneous infusion over 8 - 12 hours using electronic Microject Chrono® (Medical Technology, Turin, Italy) infusion pumps on 5 - 7 days a week.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Deferasirox (ICL670), deferoxamine (DFO)

Primary outcome measure
Safety assessments:
1. Laboratory assessments: performed monthly and included complete blood counts with differential counts:
1.1. Biochemistry testing (electrolytes, glucose, liver function tests, gamma-glutaryl-transferase, lactate dehydrogenase, cholesterol, triglycerides, uric acid, total protein, C-reactive protein, copper and zinc level)
1.2. Iron parameters (total iron, transferrin, transferrin saturation and ferritin)
1.3. Urinary testing performed on random collections (determination of creatinine, total protein and albumin)
2. Physical examinations (electrocardiograms [ECG], audiometry and ophthalmological tests) were performed at baseline, 12, 24, 36 and 52 weeks
3. In patients less than 16 years of age, additional assessments included growth velocity and pubertal stage

Secondary outcome measures
Efficacy assessments:
1. Liver iron concentration: determined by superconducting quantum interference device (SQUID) biosusceptometry at baseline, 24 and 52 weeks

2. Serum ferritin: assessed monthly during the study and the change was determined using the baseline and final ferritin level

Compliance:
1. For deferasirox, compliance was assessed by counting the number of tablets returned in bottles at each visit
2. For deferoxamine, the numbers of vials returned at each visit were counted

Overall study start date
01/01/2004

Completion date
01/01/2006

Eligibility

Key inclusion criteria
Patients with SCD requiring chronic blood transfusions to prevent complications (stroke, chest syndrome) and thus developing transfusional iron overload requiring chronic chelation therapy.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
195

Key exclusion criteria
1. Serum creatinine above the upper limit of normal (ULN)
2. Significant proteinuria (as indicated by a urinary protein:creatinine ratio of greater than or equal to 0.5 confirmed at two visits)
3. Active hepatitis B or C:
3.1. Active hepatitis B defined as liver function tests above the normal range, together with a positive antigen (hepatitis B e antigen, hepatitis B surface antigen) test or positive immunoglobulin M (IgM) core antibody test in conjunction with a negative hepatitis B surface antibody test
3.2. Active hepatitis C defined as liver function tests above the normal range in the presence of a positive hepatitis C antibody test and detectable hepatitis C ribonucleic acid (RNA) levels
4. Second and third atrioventricular block
5. QT interval prolongation
6. Therapy with digoxin or similar medications (treatment with β-blockers or angiotensin-converting enzyme inhibitors was permitted)
7. Chelation therapy-associated ocular toxicity

Date of first enrolment

01/01/2004

Date of final enrolment
01/01/2006

Locations

Countries of recruitment
Canada

France

Italy

United Kingdom

United States of America

Study participating centre
Children's Hospital & Research Center at Oakland
Oakland
United States of America
94609-1809

Sponsor information

Organisation
Novartis Pharmaceuticals Corporation (USA)

Sponsor details
One Health Plaza
East Hanover
United States of America
07936
+1 (0)862 778 2791
halyna.wysowskyj@pharma.novartis.com

Sponsor type
Industry

ROR
https://ror.org/028fhxy95

Funder(s)

Funder type
Industry

Funder Name
Novartis Pharmaceuticals Corporation

Alternative Name(s)
Novartis Pharmaceuticals Corp., Novartis United States, Novartis, NPC

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
Results article	results	01/02/2007		Yes	No