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

Submission date 23/07/2003	Recruitment status No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 05/09/2003	Overall study status Completed	 Statistical analysis plan [X] Results
Last Edited 21/03/2016	Condition category Haematological Disorders	Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s) Scientific

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Additional identifiers

EudraCT/CTIS number

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

Adull

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 angiotensinconverting 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?
<u>Basic results</u>				No	No
<u>Results article</u>	results	01/02/2007		Yes	No