A phase 2, multi-national, multi-centre, double masked, randomised, placebo controlled, parallel-group study to investigate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of darapladib administered for 3 months to adult subjects with diabetic macular edema with centre involvement (DM2115403)

Published: 20-12-2011
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Primary: efficacy, assessed by best-corrected visual acuity and SD-OCT of 1 eye (*study eye*). Secondary: retina anatomy of the study eye, safety and tolerability, PK, PD.Exploratory: Best-corrected visual acuity, SD-OCT and retina anatomy of the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Eye disorders NEC
Study type	Interventional

Summary

ID

NL-OMON35596

Source
ToetsingOnline

Brief title
DM2115403

Condition

- Eye disorders NEC

Synonym
macular edema

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline BV
Source(s) of monetary or material Support: GlaxoSmithKline BV

Intervention

Keyword: darapladib, diabetes, edema, macular

Outcome measures

Primary outcome

Best Corrected Visual Acuity and SD-OCT2 centre subfield retinal thickness in

the study eye.

Secondary outcome

Changes in retinal anatomy of the study eye, safety and tolerability, PK, PD.

Study description

Background summary

Macular edema is a major cause of vision loss in diabetic patients, which may occur at any stage of diabetic retinopathy. Sight-threatening diabetic macular edema (DME) has been managed with laser photocoagulation, and with off-label use of intravitreally administered medications such as anti-VEGF agents and corticosteroids.
In 2011 intravitreal ranibizumab was approved in Europe as the first pharmacologic therapy for DME. However, an unmet need persists driven by the need for less burdensome treatment options that ideally can also provide superior outcomes.

Darapladib is a novel, selective, orally active inhibitor of Lp-PLA2 currently under clinical development. Pre-clinical observations suggest that inhibition of Lp-PLA2, using a variety of Lp-PLA2 inhibitor compounds, may reduce diabetes-induced central nervous system (CNS) vascular permeability, including the retina.
The purpose of this study is to characterize the systemic and ocular safety and tolerability, pharmacokinetics, exploratory efficacy and pharmacodynamics of 3 months of repeat administration of oral darapladib in diabetic macular edema patients with centre involvement.

Study objective

Primary: efficacy, assessed by best-corrected visual acuity and SD-OCT of 1 eye (*study eye*).
Secondary: retina anatomy of the study eye, safety and tolerability, PK, PD.
Exploratory: Best-corrected visual acuity, SD-OCT and retina anatomy of the other eye.

Study design

Multicenter randomized double blind phase II parallel group study.
Randomisation (2:1) to treatment with:
1. Darapladib 160 mg once daily.
2. Placebo.
Treatment duration 3 months.
Stratification according to visual acuity.
50-100 patients.
Interim analysis after 10 or 20 active subjects complete 3 months of treatment with darapladib without rescue treatment.

Intervention

Treatment with darapladib or placebo.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: 6 visits and 1 phone call in approx. 19 weeks. Duration 1-4 h (1x 9 h for serial PK samples).
6x routine blood tests ca. 70 ml in total. 1x serial PK sampling with 7 samples in approx. 8 h.
Optional pharmacogenetic blood sample (1x 10 ml).
5x general ohthalmological examination, 6x SD-OCT test.
2x fundus photography.

Contacts

Public
GlaxoSmithKline BV

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Male and female patients 18 years or above with diabetic macular edema and central involvement.
* Confirmation of diagnosis in the study eye by fluorescein angiography.
* Retinal thickening > 330 microns for Heidelberg Spectralis and >310 for Zeiss Cirrus.
* Best corrected visual acuity score of 78-24 letters (Snellen equivalent ~20/32 to 20/320).
* Diabetes mellitus type 1 or 2.
* Safe contraception for women of childbearing potential.

Exclusion criteria

* Additional eye disease in the study eye that could compromise assessments.

* Active proliferative diabetic retinopathy in the study eye.
* Ischemic maculopathy (see protocol for details).
* History of choroidal neovascularization in the study eye, or current choroidal neovascularization in the fellow eye requiring treatment.
* Intraocular surgery or laser photocoagulation in the study eye within 3 months of dosing.
* Study eye: intravitreal ranibizumab within 90 days or or intraocular steroids within 180 days of dosing.
* Fellow eye: (expected need for) intravitreal bevacizumab during the study.
* Best-corrected visual acuity score by electronic ETDRS < 56 letters in the fellow eye at screening.
* Use of any systemically administered anti-angiogenic agent within 6 months of dosing.
* Uncontrolled intraocular pressure >22 mmHg in the study eye despite treatment.
* Within 6 months prior to the Screening Visit, use of medications known to be toxic to the retina.
* HbA1c >10% at screening.
* Severe asthma that is poorly controlled.
* Chronic administration of strong CYP3A4 inhibitors.
* History of or current chronic use of systemic steroids 30 days or less prior to screening.
* Breastfeeding, pregnancy.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-08-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	darapladib
Generic name:	darapladib

Ethics review

Approved WMO Date:	20-12-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-01-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-01-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-02-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	24-09-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2011-002944-28-NL
CCMO	NL38878.018.11