A phase IIIB, one year, open label, multicentre, noncomparative study to evaluate the safety and tolerability of intravitreal pegaptanib sodium injection in subjects with diabetic macular edema (DME)

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The primary objective of this study is to further evaluate the safety and tolerability of pegaptanib sodium in subjects with DME.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Interventional

Summary

ID

NL-OMON36645

Source
ToetsingOnline

Brief title
A5751036-PROJECTION

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
Diabetic Retinopathy; swelling of the retina

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diabetic macular edema, Intra-vitreale injection, Pegaptanib sodium, Phase 3b

Outcome measures

Primary outcome

The incidence of AEs both ocular and non-ocular.

Secondary outcome

- The incidence of SAEs both ocular and non-ocular.

- Mean total number of injections per subject.

- Mean changes in BCVA (Visual Acuity Assessment) from baseline to end of

treatment.

Study description

Background summary

Diabetic retinopathy is one of the leading causes of blindness in the developed world. DME is a manifestation of diabetic retinopathy that can produce loss of central vision. Data from the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) estimate that after 15 years of known diabetes, the prevalence of DME is approximately 20% in individuals with type 1 diabetes mellitus (DM), 25% in individuals with type 2 DM who are taking insulin and 14% in individuals with type 2 DM who do not take insulin. Similarly in Europe, the prevalence of proliferative diabetic retinopathy ranged from 19.7% in France to 31.5% in UK; DME was reported in approximately 10 % of subjects.
Clinically, DME is retinal thickening within 1 disc diameters of the centre of the macula, with or without lipid exudates, and with or without cystoid changes. Laser or other surgical modalities can help minimize the risk of moderate or severe vision loss. There is, however, no approved therapy for the treatment of DME in subjects who have failed to respond to laser therapy.
Pegaptanib is a VEGF antagonist currently approved for the treatment of

neovascular AMD and in development for treatment of DME. It is a pegylated oligonucleotide that binds with high specificity and affinity to the VEGF165 isoform which is preferentially involved in pathological retinal revascularization and retinal vascular permeability. It has been hypothesized that pegaptanib could play a significant role in an ocular disease such as DME by inhibiting vascular leakage.

Study objective

The primary objective of this study is to further evaluate the safety and tolerability of pegaptanib sodium in subjects with DME.

Study design

This will be an open label, multicentre, non-comparative study. Approximately 500 subject will be enrolled in the study and will be in the study for up to a maximum of 54 weeks

Intervention

All subjects will be treated in the study eye with intravitreal pegaptanib sodium 0.3 mg injection given once every 6 weeks.
Those subjects who show a clinical benefit from therapy should continue receiving intravitreal pegaptanib sodium 0.3 mg injections at the discretion of the investigator up to a maximum of 48 weeks. The interval between any subsequent injection should not be less
than 6 weeks.

Study burden and risks

Generally, pegaptanib sodium treatment appears well tolerated in humans. The majority of AEs reported in completed and ongoing studies were mild or moderate in severity and ocular in nature. The most commonly reported side effects are caused by the injection procedure itself rather than the study drug, and include: eye inflammation, eye pain, increased pressure inside the eye, small marks on the eye surface (punctate keratitis), small particles or spots in your vision (vitreous floaters or opacities).
There is a maximum of 11 visits, with an average duration of 1-2,5 hour.
Subjects undergo at 1 or more visits the following:
Urine pregnancy Test (if required in female subjects), General Medical History, History of Diabetes Mellitus, Ophthalmologic Medical History, Blood Pressure and Pulse, Visual Acuity Assessment (BCVA), Ophthalmologic Examination, and Tonometry.

Contacts

Public
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Scientific
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United States

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Evidence of a personally signed and dated informed consent document indicating that the subject (or a legally acceptable representative) has been informed of all pertinent aspects of the study.
2. Subjects who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.
3. Subjects with documented clinical diagnosis of diabetic macular edema (DME) with proliferative or non proliferative diabetic retinopathy.
4. Subjects, who according to the clinical assessment of the investigator, may benefit from anti-VEGF therapy including those subjects who were participating in the A5751013 study and who, in the investigator*s opinion, may benefit from continued pegaptanib sodium therapy.
5. Best corrected distance visual acuity in the study eye must be with a letter score between

78 and 24, inclusive (20/32 to 20/320 Snellen equivalents).
6. Intraocular pressure of 21 mmHg, or less.
7. The treating investigator should be comfortable that focal laser (direct and grid as needed) can be deferred for at least 18 weeks in the study eye, even though focal or grid laser is indicated.
8. Type I or Type II diabetic subjects as defined by the WHO criteria, of either gender, and aged >= 18 years.
9. Women must be using effective contraception or be post-menopausal for at least 12 months prior to trial entry, or surgically sterile. All women of childbearing potential must have a negative urine pregnancy test at baseline and negative urine pregnancy tests immediately prior to each injection and use an effective form of contraception during the trial and for at least 60 days following the last dose of pegaptanib sodium.
10. Clear ocular media and adequate papillary dilatation.

Exclusion criteria

1. Eyes with prior scatter (panretinal) photocoagulation within 4 months prior to baseline or anticipated scatter (panretinal) photocoagulation within the next 6 months.
2. Any other condition which could contribute or cause macular edema such as vitreous extension, vitreomacular traction or entrapment to anterior segment wound, or any retinal vein occlusion involving the macula that could, in the investigator*s opinion, preclude benefit from pegaptanib sodium treatment.
3. Atrophy/scarring/fibrosis involving the centre of the macula, including evidence of laser treated atrophy within 200 microns of foveal avascular zone (FAZ). Any known subfoveal hard exudates or retinal pigment epithelium (RPE) atrophy.
4. Subjects who have received YAG laser, or peripheral retinal cryoablation, or laser retinopexy (for retinal tears only), or focal or grid photocoagulation, within the previous 16 weeks.
5. Significant media opacities, including cataract, which might interfere with visual acuity and assessment of toxicity.
6. Any intraocular surgery within 4 months of study entry.
7. Previous vitrectomy.
8. Previously documented HbA1C level >10% or recent signs of uncontrolled diabetes (3 or more episodes of severe hypoglycaemia by DCCT (Diabetes Control and Complications Trial) definition [10] within 3 months of baseline, or 2 or more episodes of ketoacidosis within 1 year of baseline, or an episode of ketoacidosis within 3 months of baseline).
9. Known serious allergies to the components of pegaptanib sodium formulation.
10. Subjects who have received either pegaptanib sodium or any other anti-VEGF agent and have not benefited from the treatment.
11. Any of the following underlying diseases including:
- History or evidence of severe cardiac disease eg. NYHA Functional Class III or IV (eg marked limitation of activity due to fatigue, palpitation or dyspnoea, or worse), myocardial infarction within 6 months, ventricular tachyarrythmias requiring ongoing treatment or unstable angina.
- History of stroke within 12 months prior to baseline visit or evidence of clinically significant peripheral vascular disease such as intermittent claudication or prior amputation.

- Acute ocular or periocular infection.
12. Systolic BP > 160 (2 different readings) or diastolic BP > 100 (2 different readings).

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	31-01-2011
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Macugen
Generic name:	Pegaptanib sodium
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-01-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	16-03-2011

Application type:	First submission
Review commission:	METC Brabant (Tilburg)

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
EudraCT	EUCTR2010-020946-80-NL
ClinicalTrials.gov	NCT01189461
CCMO	NL34207.008.10