# Open-label Phase-4 study to examine the change of vision-related quality of life in subjects with diabetic macular edema (DME) during treatment with intravitreal injections of 2 mg aflibercept according to EU label for the first year of treatment.

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Primary objectiveTo evaluate the change in quality of life (NEI VFQ 25) in subjects with DME during the first year of treatment with aflibercept according to the EU label for DMESecondary objectives• To assess further the safety and tolerability of...

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|---|---|
| **Ethical review** | Not approved |
| **Status** | Will not start |
| **Health condition type** | Diabetic complications |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON42719

**Source**
ToetsingOnline

**Brief title**
AQUA

### Condition

- Diabetic complications
- Eye disorders NEC

**Synonym**

diabetic fluid accumulation in the macula, diabetic macular edema

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** INC Research
**Source(s) of monetary or material Support:** Industry

## Intervention

**Keyword:** aflibercept, diabetic macular edema, DME, quality of life

## Outcome measures

### Primary outcome

The primary efficacy variable is

* The change from baseline to Week 52 in the NEI VFQ 25 total score

The calculation for NEI VFQ-25 sub-scale scores and total score will be

performed according to the *NEI VFQ 25 Scoring Algorithm - August 2000*.

### Secondary outcome

The secondary efficacy variables include

* The change from baseline to Week 52 in the NEI VFQ 25 near activities subscale

* The change from baseline to Week 52 in the NEI VFQ 25 distant activities

subscale

* The change from baseline to Week 52 in BCVA (ETDRS letter score)

* The change from baseline to Week 52 in CRT measured by OCT

Proportion of subjects progressing to >= 61 ETDRS diabetic retinopathy severity

scale (DRSS) as assessed by FPExploratory efficacy variables

A complete list of variables to be analyzed for this study will be provided in

the statistical analysis plan (SAP).

The following safety variables will be assessed:

• Adverse events

• Vital signs

• Ophthalmologic safety variables

# Study description

**Background summary**

Diabetic retinopathy is a major cause of visual impairment. Diabetic macular edema (DME) is a manifestation of DR and is the most frequent cause of blindness in young and mid-aged adults. It is estimated that 4.8% of the global population has diabetic retinopathy, while 3% to 4.1% of Europeans are affected.
The detrimental impact on quality of life (QoL) from vision loss compounds any loss in QoL due to diabetes or its complications and comorbidities. This combined with the threat of further declines in visual function, or uncertain prospect of an uncomfortable treatment, may affect patients* psychological state or lead to social isolation

**Study objective**

Primary objective
To evaluate the change in quality of life (NEI VFQ 25) in subjects with DME during the first year of treatment with aflibercept according to the EU label for DME

Secondary objectives
• To assess further the safety and tolerability of aflibercept in this population
• To assess the change in the diabetic retinopathy severity score (DRSS) from baseline to Week 52
• To support patient recruitment for the EMA-requested post-approval efficacy study in DME

**Study design**

Single-arm study administering aflibercept according to EU label for the first year of treatment, i.e. 2 mg every 4 weeks for 5 consecutive doses, and dosings every 8 weeks thereafter.

### Intervention

In this single-arm study all subjects will receive aflibercept according to the EU label posology, i.e. 5 monthly intravitreal injections followed by administrations every 8 weeks

### Study burden and risks

Throughout the entire study, all subjects enrolled will receive active treatment approved for DME with close medical supervision according to established local standard of care in clinical practice.
Taken together, participation in this study is not expected to bear an incremental risk for the enrolled patients.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

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

## Inclusion criteria

• Type 1 or 2 diabetes mellitus
• Diagnosis of DME secondary to diabetes mellitus involving the center of the macula (defined as the area of the center subfield on OCT) in the study eye
• Decrease in vision determined to be primarily the result of DME in the study eye
• BCVA in the study eye of ETDRS letter score 73 to 24 (This corresponds to a Snellen equivalent of approximately 20/40 to 20/320.)

## Exclusion criteria

A subject must not meet any of the following exclusion criteria, at screening and baseline as applicable, to be eligible for enrollment into this study.
1. Previous treatment with anti-angiogenic drugs in study eye (e.g. pegaptanib sodium, bevacizumab, ranibizumab) within the last 12 weeks
2. History of vitreoretinal surgery and/or including scleral buckling in the study eye
3. Use of long acting steroids, either periocular or intraocular, in the preceding 120 days
4. Any ocular or periocular infection in the preceding 4 weeks
5. Active proliferative diabetic retinopathy (PDR), current iris neovascularization, vitreous hemorrhage, or tractional retinal detachment in the study eye
6. Aphakia in the study eye
7. Cataract surgery within 90 days
8. Yttrium-aluminum-garnet capsulotomy in the study eye within 30 days
9. Any other intraocular surgery within 90 days
10. Ocular inflammation (including trace or above) or history of uveitis in the study eye
11. Vitreomacular traction or epiretinal membrane in the study eye evident biomicroscopically or on OCT that is thought to affect central vision
12. Pre-retinal fibrosis involving the macula of the study eye
13. Structural damage to the center of the macula in the study eye that was likely to preclude improvement in BCVA following the resolution of macular edema including atrophy of the retinal pigment epithelium, subretinal fibrosis or scar, significant macular ischemia or organized hard exudates
14. Filtration surgery for glaucoma in the past or likely to be needed in the future on the study eye
15. Intraocular pressure (IOP) >= 25 mmHg in the study eye
16. Concurrent disease in the study eye, other than DME, that could compromise VA, require medical or surgical intervention during the study period, or could confound interpretation of the results (including retinal vascular occlusion, retinal detachment, macular hole, or choroidal neovascularization of any cause)
17. Myopia of a spherical equivalent prior to any possible refractive or cataract surgery of >= 8 diopters
18. Administration of systemic anti angiogenic agents within 180 days
19. Uncontrolled diabetes mellitus in the opinion of the investigator
20. Uncontrolled blood pressure (defined as systolic blood pressure > 160 mmHg or diastolic

blood pressure > 95 mmHg while subject is sitting confirmed in two separate measurements)
21. Presence of any contraindications indicated in the EU commission/locally approved label for aflibercept
22. Evidence of infectious blepharitis, keratitis, scleritis, or conjunctivitis in either eye
23. Allergy to fluorescein
24. Current treatment for a serious systemic infection
25. History of either cerebral vascular accident and/or myocardial infarction within 180 days
26. Renal failure requiring dialysis or renal transplant
27. History of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug, might affect interpretation of the results of the study, or renders the subject at high risk for treatment complications
28. Significant media opacities, including cataract, in the study eye that interferes with visual acuity, fundus photography or OCT imaging.
29. Breast-feeding women
30. Previous assignment to treatment during this study
31. Concomitant participation in another clinical study with investigational medicinal product(s).
32. Close affiliation with the investigational site; e.g. a close relative of the investigator, dependent person (e.g. employee or student of the investigational site)

# Study design

## Design

| | |
|---|---|
| Study phase: | 4 |
| Study type: | Interventional |
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Enrollment: | 6 |
| Type: | Anticipated |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |

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|---|---|
| Brand name: | aflibercept |
| Generic name: | Eylea |
| Registration: | Yes - NL intended use |

## Ethics review

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|---|---|
| Approved WMO Date: | 06-05-2015 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Not approved Date: | 30-07-2015 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

## 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 | EUCTR2014-005119-17-NL |
| CCMO | NL53088.091.15 |