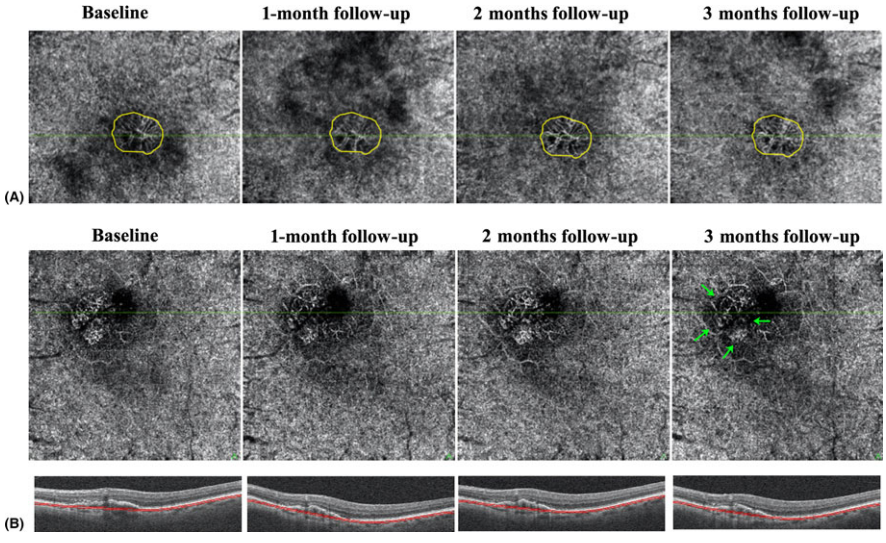

Fig. 1. Optical coherence tomography angiography (OCTA) C-scan (3 × 3) of case #04 (A) and case #06 (B – 30-μm thick) with type 2 choroidal neovascularization. (A) example of greatest area measurements (yellow lines) of the choroidal neovascularization (CNV) on sequential optical coherence tomography angiograms for subject #04. The CNV lesion does not show any significant changes over time. (B) *en face* optical coherence tomography (OCT) angiograms showing time–course of CNV after treatment with intravitreal anti-VEGF: the lesion size and the main vascular complex over do not show any significant changes over time. A reduction in the capillary network of fine vessels within the CNV is visible at the end of the follow-up (green arrows). The corresponding cross-sectional OCT B-scans with the segmentation lines (bottom) show the absence of subretinal fluid and a marked involution of the neovascular lesion after ranibizumab treatment.

Twelve eyes of 12 patients with treated type 2 CNV (mean age 75.6+/−9.4 years) for three consecutive monthly visits after the loading phase were investigated (two eyes excluded because of low-quality images). Mean duration of symptoms at time of diagnosis was 30.2+/− 27.1 days, and mean size of CNV at FA was 5.65+/−10.35 mm^2. Mean time from CNV diagnosis to the lesion being no more active was 3.9 months (average of 3.9 intravitreal injections).

Quantitative OCTA analysis revealed a CNV area of 4.99+/−3.99 mm^2 at baseline examination, which did not change significantly (5.15+/−4.27 mm^2; p = 0.99) after 3 monthly ranibizumab injections (Fig. 1A).

Qualitative OCTA analysis revealed the persistence of the main neovascular complex in 9/10 eyes (Fig. 1B). However, a subtle shrinkage of vessels at the edge of the lesion and reduction in the capillary network of fine vessels within the neovascular lesion was observed in all eyes (Fig. 1B).

No significant relationships were found between age, gender, duration of symptoms, CNV area on FA at time of diagnosis and change in CNV size on OCTA during follow-up (p > 0.05).

Our quantitative and qualitative analysis of treated type 2 CNV undergoing monthly anti-VEGF treatment reveals that while the size of the lesion as well as the main neovascular complex does not change during the short-term follow-up, the capillary plexus shows attenuation. These results suggest that anti-VEGF therapy might not be effective in reducing the main neovascular complex size possibly because of the presence of pericytes overlying the endothelial cells, even in the monthly regimen (Benjamin et al. 1998).

The main limitation could be related to the inability to be sure that the image quality of the OCTA signal in the area analysed was the same in all visits.

Our findings, in line with previous publications (Jia et al. 2014; de Carlo et al. 2015; Kuehlewein et al. 2015), suggest that OCTA can be considered as a valuable tool for monitoring treated CNV.

In conclusion, using *en face* measurements of OCTA images, we showed that further reduction in size is not seen once the type 2 CNV lesion becomes no more active.

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Switching to aflibercept in patients with neovascular age-related macular degeneration not responding to bevacizumab: a pilot study

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Editor,

Anti-vascular endothelial growth factor (VEGF) therapy has become the mainstay of neovascular

age-related macular degeneration (nAMD) treatment and has substantially improved visual prognosis. The first-line anti-VEGF agent used in the Netherlands is bevacizumab because of its superior cost-effectiveness compared to ranibizumab and aflibercept (Nederlands Oogheelkundig Gezelschap 2014). Even though bevacizumab is generally effective, approximately 10% of patients are non-responders. The effectiveness and working mechanism of bevacizumab are comparable to those of ranibizumab, both being VEGF-A antibodies (CATT Research Group et al. 2011). However, the therapeutic mechanism of aflibercept is slightly different, which functions as a decoy receptor for VEGF-A, VEGF-B and placental growth factor. Therefore, aflibercept seems like a more promising alternative than ranibizumab in case of non-response to bevacizumab. Although aflibercept is an effective treatment for nAMD (Heier et al. 2012), its role as a secondary treatment option requires further investigation. Here, we report the treatment response to aflibercept in nAMD patients who did not respond to bevacizumab treatment.

This prospective, single-arm, open-label, clinical trial was approved by the local ethical committee (NL44122.091.13) and was registered at the Dutch trial register (NTR4188). We included 10 eyes of nine patients (Table 1) who were non-responder to bevacizumab. Inclusion criteria were inadequate response to bevacizumab treatment defined as a persistent central retinal thickness (CRT) of ≥300 μm on optical coherence tomography (OCT); having received at least three bevacizumab injections within 1 year before inclusion in this study; active nAMD as seen on fluorescein angiography and OCT; maximally 2 years since start of bevacizumab treatment; 1–3 months since the last bevacizumab injection; and best-corrected visual acuity (BCVA) at baseline between 20/25 and 20/320. Patients were excluded if they had signs of subretinal fibrosis, scarring or geographic atrophy involving the center of the macula; pigment epithelial detachment with a height of ≥150 μm; or any other retinal diseases.

Table 1. Baseline characteristics.

n = 10 eyes of 9 patients	
Male, n (%)	4 (44%)
Age, median (range)	75 (55-87)
Eye included, n (%)	
Right eye	4 (40%)
Left eye	6 (60%)
Nr of bevacizumab injections, median (range)	6 (3-11)
CRT at baseline in μm, mean (SD)	540 (110)
BCVA at baseline in letters, mean (SD)	57.6 (18.7)

CRT = central retinal thickness; BCVA = bestcorrected visual acuity.

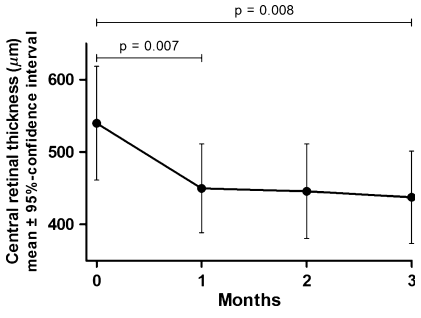

Fig. 1. Course of central retinal thickness after switching to aflibercept.

Aflibercept was administered as three consecutive monthly injections at a dose of 2 mg (0.05 ml). At every visit, we measured CRT on OCT (Spectralis HRA+OCT, Heidelberg Engineering) and ETDRS BCVA. One month after the last injection response was evaluated. All statistical comparisons were made in SPSS using a paired t-test.

Central retinal thickness (CRT) decreased significantly after switching to aflibercept with a mean of 102 ± 96 μm after 3 months (p = 0.008) (Fig. 1). The largest decrease was seen after 1 month (90 ± 83 μm, p = 0.007). Best-corrected visual acuity (BCVA) increased correspondingly with 6.7 ± 11.4 ETDRS letters, however, this was not significant (p = 0.096). The change in CRT was substantial in seven eyes, with a decrease of >50 μm. In seven of 10 eyes there was a functionally relevant improvement of >5 ETDRS letters.

In this study, there was a clear anatomical benefit of switching to aflibercept. Most eyes also improved functionally, however not significantly, likely due to a lack of power. The 3-month BCVA changes we found were good compared to other prospective studies on switching to aflibercept after non-response to previous anti-VEGF treatment, where it ranged between 0 and +7 letters after 6 months (3 month data not available for most studies) (Lazzeri et al. 2015). In these previous studies, anatomical response varied between -127 and -15 μm; however, most find CRT changes of <50 μm. An explanation for our good results could be that patients in our study were switched relatively early, sometimes as soon as after 3 months of bevacizumab treatment, leaving more room for improvement. In conclusion, this study provides additional evidence that switching to aflibercept may be beneficial after non-response to bevacizumab, resulting is anatomical as well as functional improvement.

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