BMJ Open Ophthalmology

Patient satisfaction following a switch from treat-and-extend to observe-and-plan regimen in age-related macular degeneration

Tora Sund Morken ,[1,2] Christina Knutsen,[3] Margrete Sætre Hanssen,[1,2] Dordi Austeng[1,2]

To cite: Morken TS, Knutsen C, Hanssen MS, *et al*. Patient satisfaction following a switch from treat-and-extend to observe-and-plan regimen in age-related macular degeneration. *BMJ Open Ophthalmology* 2022;**7**:e000930. doi:10.1136/bmjophth-2021-000930

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjophth-2021-000930).

Received 28 October 2021
Accepted 16 December 2021

[1]Department of Ophthalmology, St.Olav hospital, Trondheim University Hospital, Trondheim, Norway
[2]Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology (NTNU), 7491 Trondheim, Norway
[3]Faculty of Medicine and Health Sciences, NTNU, Trondheim, Norway

Correspondence to
Dr Tora Sund Morken; tora.s.morken@ntnu.no

ABSTRACT

Objective Standard treatment of neovascular age-related macular degeneration (nAMD) is intravitreal injections (IVI) of antivascular endothelial growth factor (anti-VEGF) according to treat-and-extend (TnE). Observe-and-plan (OnP), a new regimen based on each individual's relapse interval lead to fewer clinical visits and has so far shown to be safe in treatment-naïve patients. In this study, we explore patient satisfaction and safety in nAMD when switching from TnE to OnP.

Methods and analysis 38 participants treated acording to TnE for ≥12 months were included and switched from TnE to OnP with their last stable interval. Main outcome was patient satisfaction (Leeds Satisfaction Questionnaire). Secondary outcomes were best-corrected visual acuity (BCVA), central retinal thickness (CRT) before and 12 months after switch and number of monitoring visits and injections of anti-VEGF 12 months prior to and following switch.

Results Mean patient satisfaction was higher (3.7±0.5 SD) at 12 months after switch from TnE to OnP than before (3.6±0.5 SD, p=0.009, response rate 76%). BCVA and CRT were unchanged. Number of monitoring visits and injections were lower in the 12 months following than prior to switch (p<0.001).

Conclusion A switch from TnE to OnP in a non-treatment-naïve population resulted in higher patient satisfaction, while maintaining stable BCVA. This indicates that OnP may be applicable in the large group of nAMD patients that have received IVI for several years. OnP may alleviate the treatment burden on both individual and society of frequent clinical visits while increasing patient satisfaction.

Key messages

What is already known about this subject?

► Observe-and-plan (OnP) leads to fewer clinical visits than treat-And-extend (TnE) regimen in antivascular endothelial growth factor treatment of neovascular age-related macular degeneration (AMD) in treatment-naïve patients.

What are the new findings?

► This study adds that switching from TnE to OnP in a non-treatment-naïve population result in higher patient satisfaction, while maintaining stable best-corrected visual acuity.

How might these results change the focus of research or clinical practice?

► These results indicate that switching to OnP in the large population of patients that are in treatment for neovascular AMD is feasible and safe for patients.

INTRODUCTION

Current standard treatment of neovascular age-related macular degeneration (nAMD) is intravitreal injections (IVIs) of antivascular endothelial growth factor (anti-VEGF) according to treat-and-extend (TnE) protocol.[1] Following 3 monthly doses of anti-VEGF TnE elongates treatment interval as the patient remains in a stable phase of the disease. The interval is subsequently augmented in 2-week increments up to 12 weeks interval. This protocol requires one clinical visit to an eye doctor per injection, leading to approximately eight visits/year in the first year of treatment.[2] Observe-and-plan (OnP) is a protocol where the 3 monthly IVIs are followed by an observation phase where patients are controlled every month until disease relapse.[3] The regimen is based on findings that propose the individual need for retreatment is stable over time.[4 5] Treatment interval is determined by the number of weeks from loading dose until relapse minus 2 weeks and the patient then receives treatment three times prior to a new clinical visit. It is conceivable that such a treatment plan represent an improvement for the patient because of less demand for clinical visits and a treatment plan that is predictable beyond their next appointment. However, patient-related outcome measures such as satisfaction in patients switching from TnE to OnP has not earlier been described. In treatment-naïve patients OnP protocol reduces clinical

visits in the first 2 years following treatment by a half while number of IVI and best-corrected visual acuity (BCVA) is unchanged compared with TnE.[3 6] OnP, therefore, may reduce the clinical burden while maintaining patient safety in treatment-naïve nAMD patients. Furthermore, the application of OnP in a Nordic healthcare setting has not earlier been described. We hypothesised that OnP would lead to increased patient satisfaction, fewer clinical visits and comparable clinical outcomes in a population of nAMD patients that have been receiving IVI ≥12 months.

MATERIALS AND METHODS

To investigate this, we recruited participants with nAMD from the Department of Ophthalmology, St.Olav hospital, Trondheim University Hospital, Norway to perform a switch in treatment protocol from TnE to OnP. The study took place between 2 January 2017 and 31 May 2018. The participants were consecutively included from January to May 2017 and followed for a year in a prospective study. Data from previous years were collected retrospectively from patient medical records. The Norwegian national health insurance scheme has near-universal coverage of the population, and this tertiary clinic covers the population in Sør-Trøndelag County in Central Norway; about 300 000 inhabitants. The inclusion criteria were having received IVI of anti-VEGF for ≥12 months (±4 weeks) prior to switch. Exclusion criteria were non-ability to give an informed consent. At time point 1, patients switched TnE to OnP protocol and were followed prospectively with their last stable interval between IVI (figure 1). According to the OnP strategy, treatment was given with three injections with the same interval they had before the switch. If their interval was 10, 12 or 16 weeks, they received two injections before new evaluations to avoid a too long period between clinical visits. They were then evaluated by a physician to determine if their macula was dry or wet on a clinical visit. The patients who presented with a relapse of intraretinal or subretinal fluid had their interval shortened by 2 weeks.

Patient-related outcome measures was measured with the Leeds Satisfaction Questionnaire (LSQ).[7] The LSQ was sent to partipicants via regular mail to fill out in their home and return in an enclosed prepaid envelope prior to time points 1 and 2. Mean overall patient satisfaction score (from 1 to 5) averaged from six subgroups (A–F); (A) general satisfaction, (B) Provision of information, (C) empathy towards the patient, (D) technical quality and competence, (E) attitude towards the patient and (F) access and continuity. Scores >3 represent satisfaction, while <3 represent dissatisfaction. The LSQ has been translated and validated for a Norwegian population.[8] Some of the questions were rephrased to fit an ophthalmological setting. Number of visits and IVI during 12 months (±4 weeks) prior to and following switch were obtained from patient medical records. BCVA was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart[9] at inclusion (time point 1) and at 12 months (time point 2) using an ETDRS-chart at 2 m distance by the same examiner. The central retinal thickness (CRT) was automatically generated by a Cirrus HD-OCT (High definition - Optical Coherence Tomography; Carl Zeiss Meditec AG, Jena, Germany).

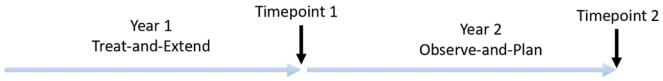

Figure 1 Switch of treatment protocol from treat and extend to observe and plan. Prior to switch participants with neovascular age-related macular degeneration had been receiveing anti-VEGF treatment for a minimal amount of 12±1 months. VEGF, vascular endothelial growth factor.

Patient involvement

Patients were involved in the design and conduct of our research. A group of 10 patients with nAMD were asked to evaluate the questionnaire (online supplemental attachment 1). In general, they thought that the questions were relevant for their situation and did not have much to add.

Statistical analyses

Data are presented as mean±SD. Statistical analyses were performed using student's paired t-test for normally distributed datasets. A $p<0.05$ was chosen as level of significance. With an estimated SD of 0.67 and a minimal clinical important difference of LSQ of 0.5, a minimum of 28 patients in each group would be needed to detect an improvement of 0.5 on LSQ with 80% power (type II error) at the 5% significance level (type I error).[8]

RESULTS

The study enrolled 38 participants and 38 eyes (all caucasian, 23 women and 15 men). The mean age was 81.2±7.4 years. Prior to protocol switch participants had been treated according to TnE for a mean amount of 3.5±2.0 years. The average treatment interval on study inclusion was 7.34 weeks±3.95. The average treatment interval after 1-year follow-up was 7.34±4.23. We had two patients on 16-week interval, six patients on 12-week interval, one patient on 10-week interval, eight patients on 8-week interval, eight patients on 6-week interval, one patient on 5-week interval and 12 patients on 4-week interval.

Twenty-nine participants (76%) answered the LSQ at both time point 1 and 2. The CRT and BCVA were obtained from all participants at both time points. Number of clinical visits and IVI in both year 1 and year 2 were obtained from 35 participants because 3 participants terminated treatment with anti-VEGF during year 2. Participants received either bevacizumab (n=12), ranibizumab (n=1) or aflibercept (n=25). In our study, only one of the patients switched drug during the follow-up time of 1 year. Overall patient satisfaction improved following switch from TnE to OnP protocol ($p=0.009$, table 1). There was no change in CRT or BCVA between time points 1 and 2 (table 2). The number of IVI was lower in year 2 (7.8±3.2) than in year 1 (9.1±2.8),

Table 1 Primary outcome

LSQ (1–5, 1=lowest score, n=29)	Time point 1	Time point 2	P value
A. General satisfaction	3.8±0.8	4.0±0.6	0.14
B. Provision of information	3.1±0.8	3.3±0.8	0.13
C. Empathy towards the patient	3.2±0.8	3.4±0.6	0.07
D. Technical quality and competence	4.3±0.6	4.3±0.6	0.96
E. Attitude towards the patient	3.4±0.6	3.5±0.6	0.14
F. Access and continuity	3.6±0.6	3.8±0.8	0.15
Overall score	**3.6±0.2**	**3.7±0.2**	**0.009**

LSQ; attachment 1 at time point 1 and time point 2. LSQ measures mean overall patient satisfaction score (from 1 to 5, 1=lowest score) averaged from six subgroups (A–F); (A) general satisfaction, (B) provision of information, (C) empathy towards the patient, (D) technical quality and competence, (E) attitude towards the patient and (F) access and continuity. Scores >3 represent satisfaction, while <3 represent dissatisfaction. Each subgroup was unchanged while the overall sum of subgroups was increased when measured at 12 months following a switch from treat-and-extend to observe and plan protocol. Results are presented as mean±SD.
LSQ, Leeds Satisfaction Questionnaire.

p=0.007). The number of clinical visits was reduced from year 1 (5.5±1.7) to year 2 (3.5±1.2, p=6,1E^{-7}).

DISCUSSION

Participants had overall higher patient satisfaction following 12 months of OnP compared with 12 months of treatment according to TnE. Furthermore, clinical visits and IVI were fewer in the year after switch of treatment regimen while clinical outcomes were unchanged, indicating that the disease remains in a stable phase despite reduced surveillance. Our findings suggest that a switch to OnP is safe not only in treatment-naïve nAMD as earlier reported,[3 6 10] but also in patients that have already received anti-VEGF because of nAMD for years. The latter group represent the largest proportion of AMD patients and the relevance of these results are therefore considerable.

To the best of our knowledge, this is the first study reporting patient reported outcome measures in a population of nAMD switching treatment regimen from TnE to OnP. The response rate in this study was high, at 76%. Limitations are that data from year 1 was collected retrospectively and that participants received all three available anti-VEGFs (bevacizumab, ranibizumab or aflibercept) which does not represent a uniform data material, but that nevertheless reflects the real-world setting of a clinical practice.

OnP is a novel treatment protocol that provides long-term treatment plans to patients. It is conceivable that this provides the patient with more self-control of their disease and more opportunity to plan ahead. This may be reflected in the overall higher patient satisfaction measured 12 months after switch of treatment regimens. Furthermore, OnP reduced the number of clinical visits and IVI, which may be perceived by the individual as a life quality improvement, given that the disease remain in stable phase.

A concern in OnP is the possibility of late recurrence following the long initial observation period. Gianniou *et al* reported two such late recurrence during a 2-year observation period of 115 eyes,[6] while Parvin *et al*[10] reported no study-regimen related complications during their 2-year observation of 112 eyes following an OnP regimen. In this study design, an initial observation period is not applied since the switch was performed using the participants last stable interval. A randomised controlled trial is needed to answer whether there is an increased risk of late recurrence in OnP compared with TnE.

Table 2 Secondary outcomes

	Time point 1 (n=38)	Time point 2 (n=38)	P value
BCVA	62.3±15.1	61.6±16.3	0.7
CRT	227.5±47.7	233.1±55.5	0.4
	Year 1 (n=35)	**Year 2 (n=35)**	**P value**
Clinical visits	5.5±1.7	3.5±1.2	6.1E-07
IVI	9.1±2.8	7.8±3.2	0.007

Best-corrected ETDRS visual acuity (BCVA) and CRT did not change from time point 1 to time point 2. During the 12 months prior to switch from TNE to OnP number of clinical visits and IVI was higher than during 12 months after switch of protocols. Results are presented as mean±SD.
BCVA, best-corrected visual acuity; CRT, central retinal thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; IVIS, intravitreal injections; OnP, observe-and-plan; TnE, treat-and-extend.

CONCLUSION

This study shows that a switch from TnE to OnP regimen results in higher patient satisfaction, with stable functional results. This implies that OnP is applicable not only in treatment-naïve patients, but also in the large group of patients that have received IVI for years. OnP may alleviate the burden on both individual and society of frequent clinical visits while increasing patient satisfaction.

Acknowledgements Alietha Vorren, MD, is acknowledged for her participation in data analyses of LSQ.

Contributors TSM and DA conceived and designed the study. All authors collected, analysed and interpreted the data and share overall responsibility. TSM is the author acting as guarantor. She accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Funding This study received innovation funding by the Central Norway Regional Health Authority.

Disclaimer The funding organisation had no role in the design or conduct of this research.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval The study adheres to the Tenets of the Declaration of Helsinki and the Regional Committee for Medical and Health Research Ethics Central (REK) has evaluated the study (2016/1610/REK midt). The study was reported to the Data Protection Officer at St.Olav hospital (Reference no. 898610).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

ORCID iD

Tora Sund Morken http://orcid.org/0000-0001-5876-284X

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