



Aflibercept 8 mg for diabetic macular edema and neovascular age-related macular degeneration: an italian expert consensus paper

Francesco Bandello¹ · Enrico Borrelli^{2,3} · Sandro De Falco⁴ · Alessandro Invernizzi^{5,6} · Paolo Lanzetta^{7,8} · Marco Lupidi⁹ · Edoardo Midena¹⁰ · Federico Ricci¹¹ · on behalf of the Eight Consensus Group

Received: 17 June 2026 / Revised: 10 August 2026 / Accepted: 15 August 2026
© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2026

Abstract

Purpose To provide consensus recommendations on the clinical use of aflibercept 8 mg in managing neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME) in the real-world setting.

Methods A modified Delphi study was undertaken, involving ophthalmologists from specialized centers in Italy, to gauge consensus on statements related to the use of aflibercept 8 mg in nAMD and DME. Two initial rounds of online surveys were conducted, followed by 2 workshops to assess the clinical feasibility of selected statements and identify the behavioral drivers and barriers to their adoption in practice. Consensus was defined as $\geq 75\%$ agreement ('strongly agree' or 'somewhat agree').

Results Consensus was reached for 30 initial statements, following refinement and discussion. Of these, 12 statements were analyzed and discussed at the behavioral workshop. Statements covered clinical differentiation of aflibercept 2 mg and 8 mg, treatment initiation in aflibercept-naïve patients, switching to aflibercept 8 mg, optimal aflibercept 8 mg maintenance, and safety considerations. There was expert group consensus that aflibercept 8 mg represents a viable treatment option with an extended injection interval for patients with nAMD or DME, with the possibility of improving treatment adherence, and therefore outcomes. Experts also discussed practical considerations in Italy and offered evidence-based guidance.

Conclusion Experts agreed that aflibercept 8 mg is a treatment option for both nAMD and DME with the potential to improve treatment adherence. Although real-world data are limited, experts offered guidance on the management of nAMD and DME in the context of aflibercept 8 mg.

Key messages

What is known

- Aflibercept 8 mg supports extended dosing intervals of up to 24 weeks in patients with nAMD and DME, with comparable visual outcomes and a similar safety profile as aflibercept 2 mg dosed at 8-week intervals

What is new

- A modified Delphi study was undertaken, involving 17 ophthalmologists from specialized centres in Italy, to gauge consensus and provide guidance on the use of aflibercept 8 mg in nAMD and DME, including the clinical differentiation of aflibercept 2 mg and 8 mg, criteria for treatment initiation, switching to aflibercept 8 mg, maintenance and safety considerations.
- In addition, recommendations are provided that may help improve clinical applicability of the provided guidance for the treatment of patients with nAMD and DME in Italy. Among others, recommendations include: Strengthening clinical training programs to emphasize the importance of treatment extension in appropriate patients; cultivating a sense of urgency among healthcare providers on the need for early diagnosis and treatment of nAMD to prevent irreversible loss of vision; and strengthening patient education to promote understanding and to improve adherence.

Keywords Diabetic macular edema · Neovascular age-related macular degeneration · Aflibercept 8 mg · High dose · Anti-VEGF

Extended author information available on the last page of the article

Introduction

Diabetic macular edema (DME) and neovascular age-related macular degeneration (nAMD) are leading causes of vision loss and blindness in adults, imposing substantial burdens on patients, caregivers, and health systems [1, 2]. The projected global prevalence of nAMD in 2040 is 288 million and 29 million for DME by 2045 [3, 4]. With the incidence of both conditions being age-related, the burden is expected to rise substantially over time as the global population ages.

Intravitreal anti-vascular endothelial growth factor (VEGF) therapy has transformed the management of DME and nAMD by slowing disease progression and substantially improving visual outcomes, and it is widely considered the standard of care [5]. Commonly used agents include ranibizumab, aflibercept, bevacizumab (off-label), faricimab, and brolucizumab; all of which typically require ongoing intravitreal injections with close monitoring, with patients receiving maintenance therapy at intervals ranging from every 4 weeks to up to 16 weeks (up to 20 weeks for brolucizumab in nAMD) [1, 6]. However, regular intravitreal anti-VEGF administration carries disadvantages: high visit and injection frequency can result in adherence challenges; logistical and financial burdens on the healthcare system; as well as emotional and psychological impact on patients [7–9]. To reduce the treatment burden, a high-dose formulation of intravitreal aflibercept 8 mg was developed to allow extended dosing intervals [10–12]. The increase in molar dose allows for prolonged VEGF suppression and potential maintenance treatment of patients at intervals of up to 24 weeks after an initial loading phase of monthly treatment [13, 14].

Aflibercept 8 mg was approved based on the CANDELA and PULSAR trials in patients with nAMD, and the PHOTON trial in patients with DME, which demonstrated efficacy comparable to aflibercept 2 mg. These studies showed that aflibercept 8 mg supports extended dosing intervals of up to 24 weeks during the maintenance phase, in patients with nAMD and DME, compared with the standard 8-week intervals for the 2 mg dose, with non-inferior visual outcomes achieved at week 48. Despite the increased dose and injection volume, these studies, with up to 96 weeks of follow-up, show a similar safety profile and no new safety signals compared with the 2 mg group [10–13].

Several key questions around the use of aflibercept 8 mg remain, such as the identification of appropriate patient populations, optimization of dosing intervals, establishment of best practices for treatment switching, and implementation of ongoing monitoring through optical coherence tomography (OCT) and visual acuity assessments. Furthermore, addressing potential safety concerns associated with the increased injection volume – such as potential risk of elevated intraocular pressure – is essential to ensure that

aflibercept 8 mg provides meaningful outcomes in real-world practice.

In this article we aim to provide practical guidance on the use of aflibercept 8 mg in managing nAMD and DME in real-world clinical settings. We also explore behavioral factors influencing the application of our guidance, to identify potential solutions that may help improve the clinical applicability of our recommendations for the treatment of nAMD and DME patients in Italy.

Methods

To provide recommendations on the clinical use of aflibercept 8 mg in nAMD and DME, a modified Delphi approach [15] was taken, involving a panel of 17 ophthalmologists from specialized centers in Italy (Appendix 1), in meetings convened and funded by Bayer. A leading panel of 8 clinical experts (Appendix 2) defined the scope of the consensus and drafted initial statements based on their clinical experience and published literature. A third-party agency (The Bloc Milan; funded by Bayer) assisted in the collation and qualitative/quantitative analysis of the survey responses, and the development of the manuscript, under the guidance of the authors. Bayer was not involved at any stage of the Delphi consensus apart from providing a courtesy review during the development of the manuscript.

The panel was invited to vote anonymously online on each statement to gauge consensus. The level of agreement or disagreement on each statement was expressed on a Likert-type scale (1=strongly agree, 2=somewhat agree, 3=neither agree nor disagree, 4=somewhat disagree, and 5=strongly disagree). Explanations were requested only for responses indicating strong disagreement (5=strongly disagree). Consensus for each statement was considered achieved when $\geq 75\%$ of respondents answered either 'strongly agree' or 'somewhat agree'. The first online vote was held on May 26, 2025. Statements that did not achieve consensus were reviewed, modified, and revoted online on June 9, 2025.

Following the panel's agreement on the statements, 2 workshops were conducted on July 15 and July 17, 2025, to assess the clinical feasibility of selected statements and identify the behavioral drivers and barriers to their adoption in practice. A total of 7 experts (Appendix 3) attended, across the 2 workshops. The process was divided into 3 phases. The first phase was to select statements of clinical importance and transform them into observable and actionable behavior. The second phase involved brainstorming factors that influence specific behavior. This step was carried out based on the COM-B (Capability, Opportunity, Motivation – Behavior) model [16, 17], which is widely used in behavioral sciences to understand and modify behaviors. Capability encompasses clinicians' and patients' knowledge, cognitive

skills, and psychological readiness. Opportunity refers to environmental and systemic enablers or constraints, such as care infrastructure and interprofessional collaboration. Motivation reflects beliefs, emotional drivers, and personal goals that guide decisions [17]. The third phase involved ideation of solutions to facilitate the performance of the desired behavior based on the behavior change wheel [17].

Results and discussion

A total of 30 consensus statements were proposed, covering the clinical differentiation of aflibercept 2 mg and 8 mg, criteria for treatment initiation, switching to aflibercept 8 mg, maintenance, and safety considerations. All statements were refined as required, discussed, and subsequently achieved consensus (Table 1), with just one statement (statement 23) requiring amendments and a second round of voting. Of these, 12 statements were subsequently analyzed and discussed at the behavioral workshop (Supplementary Tables 1–11). It is noted that Statements 2 and 30 achieved just over 75% consensus and thus, may need to be interpreted with caution.

Clinical differentiation of aflibercept 2 mg and 8 mg

Aflibercept 8 mg was developed to provide prolonged VEGF suppression, thereby reducing the dosing frequency required for the treatment of nAMD and DME.

In the pivotal Phase III PULSAR study, adults with nAMD were randomized 1:1:1 to aflibercept 8 mg every 12 weeks (Q12W), aflibercept 8 mg every 16 weeks (Q16W), or aflibercept 2 mg every 8 weeks (Q8W), following 3 initial monthly doses in all groups [12, 13]. From week 16, patients in the aflibercept 8 mg groups had their dosing interval shortened if prespecified dose regimen modification criteria denoting disease activity were met. Dosing intervals in patients receiving 8 mg could be shortened in Years 1 and 2, or extended in Year 2 based on prespecified criteria, with a minimum dosing interval of 8 weeks and a maximum of 24 weeks [13]. Clinically, aflibercept 8 mg administered Q12W or Q16W after 3 initial monthly injections achieved non-inferior gains in best-corrected visual acuity (BCVA) compared with aflibercept 2 mg Q8W after 3 initial monthly injections. Specifically at 48 weeks, the mean BCVA change from baseline was + 6.7 and + 6.2 letters for the aflibercept Q12W and Q16W groups, respectively, and + 7.6 letters for the aflibercept 2 mg group; with the difference in least square mean changes from baseline to week 48 within the non-inferiority margin of 4 letters [12]. Efficacy was maintained through week 96 of PULSAR, with mean BCVA gains of + 5.6 and + 5.5 versus + 6.6 letters for the aflibercept 8 mg Q12W and Q16W groups versus aflibercept 2 mg, respectively [13].

In the pivotal Phase II/III PHOTON study, adults aged 18 years or older with type 1 or 2 diabetes and center-involved DME were randomly assigned (1:2:1) to intravitreal aflibercept 2 mg Q8W, aflibercept 8 mg Q12W, or aflibercept 8 mg Q16W, following initial monthly dosing. From week 16, dosing intervals for the aflibercept 8 mg groups were shortened if patients met prespecified dose regimen modification criteria denoting disease activity. Dosing intervals in patients receiving 8 mg could be shortened in Years 1 and 2, or extended in Year 2 based on prespecified criteria; the minimum dosing interval was 8 weeks and a maximum of 24 weeks [18]. The PHOTON study in patients with DME reported similar results to PULSAR, with non-inferior BCVA gains for the aflibercept 8 mg arms compared with aflibercept 2 mg at week 48, with mean changes of + 8.8 letters for the aflibercept 8 mg Q12W group, + 7.9 letters for the aflibercept 8 mg Q16W group, and + 9.2 letters for the aflibercept 2 mg Q8W group [11]. Efficacy was maintained through week 96 of PHOTON, with mean BCVA gains of + 8.8 and + 7.5 versus + 8.4 letters for the aflibercept 8 mg Q12W and Q16W groups versus aflibercept 2 mg, respectively [18]. In both studies, more than 40% of patients in the aflibercept 8 mg arms achieved a last assigned dosing interval of at least 20 weeks at week 96 [13, 18]. Reassuringly, both studies showed comparable safety outcomes between the aflibercept 8 mg and 2 mg groups with similarly low rates of intraocular inflammation [11, 12].

Extending dosing intervals has been desirable in the management of DME and nAMD [19, 20]; in fact, frequent injections have been associated with reduced adherence which can result in poorer outcomes for patients [20].

Based on available data, aflibercept 8 mg has the potential of offering patients less frequent dosing compared with aflibercept 2 mg, without compromising treatment outcomes. However, there is an unmet need for more real-world data to offer education and guidance on the use of aflibercept 8 mg in clinical settings (Supplementary Tables 1 and 2).

Criteria for treatment extension post-loading in aflibercept-naïve patients (nAMD and DME)

Treat-and-extend (T&E) is the preferred strategy for initiating anti-VEGF therapy among patients with nAMD and DME because it proactively manages the disease, while allowing the extension of treatment intervals and reducing the overall number of clinic visits [21–24]. As with other anti-VEGF therapies, the T&E strategy should be considered with aflibercept 8 mg treatment after the loading phase where possible. However, some centers may not have the capacity to closely follow and monitor patients, and in such cases, where a T&E strategy cannot be implemented, a more

Table 1 Consensus statements

	Consensus statements	Level of agreement %	Behavioral analysis
	Clinical differentiation of aflibercept 2 mg and 8 mg		
1	Aflibercept 8 mg exhibits prolonged intraocular VEGF suppression, with pharmacokinetic modelling indicating active drug levels lasting up to 16 weeks – significantly longer than the 4–8-week window of aflibercept 2 mg, as demonstrated in the PULSAR and PHOTON trials.	88.2	Suppl. Table 1
2	While the majority of patients achieve disease control with aflibercept 8 mg on Q12–Q16W intervals, data from the PULSAR and PHOTON trials indicate that more than 20% of patients have a Q24W assigned treatment interval even at 156 weeks of follow-up. Therefore, extending treatment intervals beyond 16 and up to 24 weeks may be clinically justified and should be pursued where feasible.	76.5	
3	The extended dosing intervals enabled by aflibercept 8 mg may reduce treatment burden and improve adherence, both of which are recognized predictors of real-world outcomes.	94.1	Suppl. Table 2
	Criteria for treatment initiation post-loading in aflibercept-naïve patients (nAMD and DME)		
4	Treat-and-extend represents a clinically preferred strategy for aflibercept 8 mg, enabling personalized interval optimization post-loading. In settings with logistical constraints or limited follow-up capacity, fixed aflibercept 8 mg dosing offers a pragmatic approach to implement the treat-and-extend regimen.	94.1	
5	In nAMD, the PULSAR trial demonstrated that a large majority of patients can begin post-loading extension at Q12W and further extend up to Q16W, though Q8W can be applied as a conservative starting point for interval individualization.	94.1	Suppl. Table 3
6	In DME, post-loading extension to Q12W with aflibercept 8 mg is supported by the PHOTON trial in over 90% of patients, suggesting that Q12W may be a viable initial interval. In settings with logistical constraints or limited follow-up capacity, fixed aflibercept 8 mg dosing offers a pragmatic approach to implement the treat-and-extend regimen.	94.1	Suppl. Table 4
7	Post-loading intervals with aflibercept 8 mg should be individualized based on quantifiable markers of disease activity – primarily retinal fluid dynamics and visual acuity – while considering patient-specific treatment history.	100	
	Why and how to switch from an aflibercept 2 mg to an aflibercept 8 mg regimen		
8	Patients on aflibercept 2 mg could be transitioned to aflibercept 8 mg as able, subject to clinical discretion, cost and access considerations, and patient preference, unless not indicated by the SmPC.	82.3	Suppl. Table 5
9	nAMD or DME patients treated with aflibercept 2 mg who exhibit persistent fluid or require injection intervals < Q8W may be transitioned to aflibercept 8 mg, starting with a loading phase to optimize response.	82.3	Suppl. Table 6
10	For patients who are stable on aflibercept 2 mg and whose QoL is strongly affected by injection frequency or visit burden, switching to aflibercept 8 mg may extend injection intervals without compromising efficacy.	94.1	
11	Patient responders to ≥Q8W aflibercept 2 mg may be transitioned to aflibercept 8 mg, without a loading phase.	82.3	Suppl. Table 7
12	Patient responders to ≥Q8W aflibercept 2 mg may be transitioned to aflibercept 8 mg at the next already scheduled injection, with the goal of further extending intervals using either a treat-and-extend or fixed strategy.	82.3	Suppl. Table 8
	Why and how to switch from other anti-VEGF agents to aflibercept 8 mg in a patient currently treated with other anti-VEGF agents		
13	Aflibercept 8 mg is considered a valid option for patients with nAMD or DME with suboptimal anatomical and/or functional response to other anti-VEGF agents.	100	
14	Patients requiring frequent (< Q8W) injections with other anti-VEGF agents due to persistent or recurrent exudation may be transitioned to aflibercept 8 mg, starting with a loading phase to optimize response.	100	
15	Aflibercept 8 mg's broader binding profile – including VEGF-A, VEGF-B, and PlGF – could provide additional benefit in patients unresponsive to anti-VEGF agents with a narrower spectrum of action, although clinical differences, compared with other agents, remain under investigation.	94.1	
16	In nAMD patients unresponsive to other anti-VEGF agents, a large proportion of patients can begin post-loading extension at Q12W and further extend up to Q16W, though Q8W remains a conservative starting point for interval individualization. In settings with logistical constraints or limited follow-up capacity, fixed aflibercept 8 mg dosing offers a pragmatic approach to implement the treat-and-extend regimen.	88.2	
17	In DME patients unresponsive to other anti-VEGF agents, post-loading extension to Q12W with aflibercept 8 mg could be considered a reasonable initial interval. In settings with logistical constraints or limited follow-up capacity, fixed aflibercept 8 mg dosing offers a pragmatic approach to implement the treat-and-extend regimen.	94.1	
	Why and how to switch from steroids to aflibercept 8 mg in a patient currently treated with steroids		
18	Aflibercept 8 mg is a viable option in DME patients receiving intravitreal steroids for whom switching to an anti-VEGF is clinically indicated due to poor/no response in functional and/or anatomical parameters, or steroid-related side effects.	94.1	
19	In steroid-refractory DME patients who respond to aflibercept 8 mg loading doses, post-loading extension to Q12W with aflibercept 8 mg is a viable initial interval. Potential further interval extension using a treat-and-extend regimen should be based on the stability of fluid and vision.	94.1	

Table 1 (continued)

	Consensus statements	Level of agreement %	Behavioral analysis
20	In steroid-refractory DME patients who respond to aflibercept 8 mg loading doses, post-loading extension to Q12W with aflibercept 8 mg is a viable initial interval. In settings with logistical constraints or limited follow-up capacity, fixed aflibercept 8 mg dosing offers a pragmatic approach to implement the treat-and-extend regimen. Optimal aflibercept 8 mg pathway during the maintenance phase	94.1	
21	Treatment intervals with aflibercept 8 mg should be gradually extended toward the longest interval that maintains disease stability, ideally up to 16 weeks, and potentially 20–24 weeks in all patients.	100	Suppl. Table 9
22	Injection intervals should be tailored to optimize both disease control and patient quality of life, with extension guided by stability of fluid and visual function.	100	
23	In nAMD, any increase in intraretinal fluid should prompt shortening of the treatment interval, even in the absence of visual decline; whereas stable residual subretinal fluid may be tolerated before changing the treatment schedule.	82.3	Suppl. Table 10
24	Due to extended visit intervals with aflibercept 8 mg, patients should be educated to recognize signs of visual decline and, when feasible, supported with practical indications and home monitoring tools to help detect early disease recurrence.	82.3	
25	Clinical assessments during follow-up should be equally rigorous for both aflibercept 2 mg and 8 mg, as treatment potency does not obviate the need for regular imaging and functional evaluation. Safety considerations about aflibercept 8 mg	94.1	
26	The safety profile of aflibercept 8 mg is comparable to that of aflibercept 2 mg, as confirmed in the PULSAR and PHOTON trials, with no meaningful increase in serious ocular and non-ocular adverse events.	88.2	
27	Patients should be instructed to promptly report symptoms suggestive of inflammation, vision changes, and floaters, to ensure early detection of adverse events.	94.1	
28	Although the incidence of intraocular inflammation with aflibercept 8 mg is low and comparable to aflibercept 2 mg, clinicians should remain vigilant for signs of anterior or posterior segment inflammation.	88.2	
29	The 70 µL volume of aflibercept 8 mg has not been associated with permanent increase in IOP, as confirmed by available clinical trials and real-world evidence; however, additional attention should be given in case of co-existing glaucoma.	88.2	Suppl. Table 11
30	Administering aflibercept 8 mg at a slower injection speed may attenuate the transient IOP spike associated with the higher injection volume, although there is no conclusive evidence to support this.	76.5	

Based on Oxford Centre for Evidence-Based Medicine's 2011 Levels of Evidence [51]

DME diabetic macular edema, IOP intraocular pressure, nAMD neovascular age-related macular degeneration, PIGF placental growth factor, Q8W once every 8 weeks, Q12W once every 12 weeks, Q16W once every 16 weeks, Q24W once every 24 weeks, QoL quality of life, SmPC Summary of Product Characteristics, VEGF vascular endothelial growth factor

proactive fixed-dose regimen could be considered over a reactive pro re nata regimen [25].

In the PULSAR trial in patients with nAMD, the injection intervals started at 12 or 16 weeks after the 3 initial monthly doses, with 79% of patients in the aflibercept 8 mg Q12W group and 77% of patients in the aflibercept 8 mg Q16W group maintaining their assigned dosing regimen up to 48 weeks. This suggests that an initial 12-week injection interval after initial monthly injections may be feasible in most cases, with the potential to extend further in some patients [12]. However, given that the results are based on a clinical trial, which may not have accounted for the diversity of real-world clinical scenarios, it is possible that some may prefer a more conservative interval (e.g. 8 weeks) to monitor response before extending intervals.

Similarly, for DME, the PHOTON trial showed that 91% of patients maintained their assigned 12-week interval and 89% of patients maintained their assigned 16-week intervals after initial monthly injections [11]. This suggests the

potential to extend the treatment frequency of aflibercept 8 mg to Q16W in appropriate patients.

Regardless of whether it is for patients with nAMD or DME, treatment intervals with aflibercept 8 mg should be personalized based on quantifiable markers of disease activity, such as retinal fluid presence/fluctuations detected using OCT, and visual and anatomical assessments [23, 24, 26, 27]. Assessments can be performed at 8–12 weeks after the initial monthly injections, and at regular intervals thereafter, to ensure close monitoring and timely intervention if required (Supplementary Tables 3 and 4). Specifically, guidance on fluid assessment may be needed for ophthalmologists to objectively assess patients and guide decision making. While an extended dosing regimen is generally welcomed, behavioral analysis found that it may complicate logistical arrangements for some healthcare facilities. Guidance on a flexible organizational approach may help clinics devise a logistically feasible plan that allows for tailored patient management. There is also an opportunity to

reinforce education on the natural progression of nAMD and DME to ensure extended treatment intervals do not compromise outcomes.

Why and how to switch from an aflibercept 2 mg to an aflibercept 8 mg regimen

Aflibercept 8 mg has been shown clinically to allow effective treatment at intervals greater than Q12–16 W after the initial monthly injections [11, 12], which could potentially lead to improved adherence and treatment outcomes [27–29]. Switching from aflibercept 2 mg to aflibercept 8 mg may, therefore, be considered in patients who have responded to, or are responding to, aflibercept 2 mg (i.e. patients with stable disease, defined clinically as 2–3 visits with a dry retina and stable visual acuity following a treatment regimen up to the maximal extension based on the posology of the drug). However, this is subject to clinical discretion and varies between individual patients, considering safety considerations, cost/access, and patient preference.

Patients who have responded to aflibercept 2 mg but have exhibited persistent fluid (presence of fluid in 3 consecutive monthly visits) [30] or that required a treatment interval shorter than Q8W may benefit from a higher dose regimen. Among these patients, it is advisable to start with initial monthly injections after the switch, followed by a maintenance dosing of once every 8 weeks until stable disease is achieved. While some clinicians may prefer switching to another molecule in the presence of fluid, the fact that the patient had responded initially to aflibercept suggests a possibility of continued benefit from aflibercept at a higher dose (Supplementary Tables 5 and 6). In this assessment, both the amount and type of persistent fluid may influence the clinician's treatment decision—for instance, intraretinal fluid may be less tolerated, as it is associated with poorer visual outcomes.

For patients who have responded to and achieved stable disease with aflibercept 2 mg, switching to aflibercept 8 mg may allow extended treatment intervals without compromised outcomes. In this scenario, switching from aflibercept 2 mg may not require loading doses of aflibercept 8 mg, but rather a single dose administered at the previous treatment interval, with subsequent extension or reduction of the interval based on clinical findings. Inevitably, switching among stable patients may involve adaptation from clinicians and patients, as well as administrative or logistical adjustments, and therefore the switch may be more advisable for patients whose quality of life or adherence are affected by injection frequency [31]. Importantly, switching therapy should be a shared decision between clinicians and patients, and should be individualized based on clinical conditions and patient preference (Supplementary Tables 7 and 8) [32].

Why and how to switch from other anti-VEGF agents to aflibercept 8 mg

According to the UK Royal College of Ophthalmologists commissioning guidance for AMD, switching an anti-VEGF therapy is indicated for patients who have a suboptimal response after the loading phase, or at any other point due to resistance to the current agent, or in cases of allergy or presumed tachyphylaxis [30]. In this context, suboptimal response is defined as 'intraretinal fluid or subretinal fluid on OCT, other anatomic features of active or worsening disease (e.g., new subretinal hyperreflective material or new hemorrhage), or unchanged (≤ 5 -letter improvement)/reduced VA due to nAMD, after three consecutive monthly intravitreal injections. In such cases, switching to an alternative anti-VEGF therapy, including aflibercept 8 mg, is a viable strategy. While the choice of therapy is beyond the scope of the present paper, the decision should take account of multiple factors such as response to prior therapy, patient condition and preference, cost, and other regulatory or logistical considerations. It is worth noting that the broad binding profile of aflibercept allows it to bind to and inhibit multiple members of the VEGF family, including VEGF-A, VEGF-B, and placental growth factor (PlGF).

Switching to aflibercept 8 mg may also be appropriate to reduce treatment burden, especially among patients who are unable to adhere to existing treatment schedules [30]. While switching in these cases may theoretically be made on a matched treatment interval [30], we recommend starting with a loading phase to optimize results and adjusting the treatment interval during the maintenance phase via a T&E approach.

Why and how to switch from steroids to aflibercept 8 mg in patients with DME

Intravitreal corticosteroids have been shown to improve vision in patients with DME but their effect can be modest [24, 33]. Therefore, aflibercept 8 mg is a viable treatment option for patients with DME who have had a suboptimal functional or anatomical response, or steroid-related side effects with intravitreal corticosteroid treatment. However, it is important to consider the potential systemic adverse events associated with intravitreal anti-VEGF therapy in patients with diabetic retinopathy [34], necessitating individualized risk assessment. Data are lacking regarding combination therapy with aflibercept 8 mg and steroids, as well as the timing of use of aflibercept 8 mg in the context of intravitreal steroids. In the PHOTON trial, a 16-week wash-out was required for patients who had received intraocular steroids [11]. However, some experts recommend using aflibercept 8 mg immediately after steroid treatment.

For steroid-refractory DME patients responding to aflibercept 8 mg loading doses, a post-loading regimen of aflibercept 8 mg Q12W is considered a reasonable initial approach, with subsequent adjustment to treatment intervals through a T&E strategy based on fluid and vision stability. Fixed dosing at Q8W may also be employed in clinical settings with logistical constraints or limited follow-up capacity, though this approach may not be practical for all patients.

Optimal aflibercept 8 mg treatment frequency during the maintenance phase

It is reasonable to suggest that aflibercept 8 mg treatment intervals should be extended gradually to the longest interval that allows sustained disease control, ideally a frequency of Q16W or potentially up to Q24W. An increase in treatment interval reduces the treatment burden on patients and healthcare systems, whilst maintaining vision gains and fluid control [35]. The high burden of frequent injections has been associated with non-adherence to anti-VEGF treatment in both nAMD and DME [36], thus increasing treatment intervals may improve long-term patient adherence to treatment and lead to better outcomes [29]. However, it is important that extension decisions carefully weigh the capability and capacity for ongoing monitoring, especially where resources for frequent follow-up visits are limited. Failing to adequately monitor patients could result in missing early detection of fluid accumulation that would otherwise trigger an increase in treatment frequency. Inadequate monitoring can therefore lead to under-treatment and worse outcomes for patients, potentially including permanent vision loss [29, 37]. Monitoring is also important in the timely detection of serious, albeit rare, treatment complications including endophthalmitis or retinal detachment [23]. Fluid stability according to OCT remains the primary guide for interval adjustments, with visual acuity changes considered less directly linked to disease activity [38].

An earlier version of a statement regarding the indicator for shortening treatment interval with aflibercept (statement 23) failed to gain consensus during the first meeting. The original statement, “*Any increase in intraretinal fluid should prompt shortening of the treatment interval, even in the absence of visual decline, whereas an increase in subretinal fluid may be tolerated before changing the treatment schedule*”, did not reach consensus because of disagreement regarding the significance of an increased amount, or the presence, of subretinal fluid. It was agreed, however, that unchecked fluid recurrence can lead to suboptimal visual outcomes [39]. It was eventually agreed that an increase, especially if progressive, can indicate underlying disease activity and risk of visual impairment [39]. Hence, the statement was revised to reflect that increases in intraretinal fluid

volume are undesirable but stable residual subretinal fluid (defined as fluid which persists without significant fluctuation over consecutive visits, and without other signs of disease activity [i.e. no intraretinal fluid, new retinal hemorrhage, subretinal hyperreflective material, or pigment epithelial detachment], and is associated with stable visual acuity) may be tolerated without needing to change the treatment schedule. However, continued close monitoring is recommended to ensure timely intervention.

In the absence of widely available and well-established home monitoring devices, patients should be educated on detecting potential adverse events and early signs of visual decline. Clinical follow-up should remain rigorous with regular OCT imaging and functional evaluations of visual acuity to ensure ongoing disease control.

Aflibercept 8 mg safety considerations

The safety profile of aflibercept 8 mg was comparable to that of aflibercept 2 mg in both the PULSAR and PHOTON studies, with similar rates of serious ocular or systemic adverse events observed among patients receiving the higher dose [11, 12]. A network meta-analysis based on a systematic literature review of anti-VEGF therapies in nAMD did not identify any significant differences between aflibercept 8 mg and comparators in safety outcomes [40].

The 70 µL injection volume of aflibercept 8 mg has been a theoretical concern, particularly regarding increases in intraocular pressure (IOP), but clinical trials have shown that the increases were comparable to aflibercept 2 mg and were transient [11, 12]. Further observational studies have demonstrated that transient IOP elevations following aflibercept 8 mg decreased progressively post-injection [41, 42]. Although some experts suggest slower injection speeds might reduce spikes, there is no conclusive evidence supporting this. Practices such as anterior chamber tap are recommended in specific cases [43, 44]. It is noted that patients with pre-existing glaucoma should be closely monitored during treatment with aflibercept 8 mg [41].

Incidences of intraocular inflammation were low and comparable with both doses of aflibercept in clinical trials [11, 12]. A retrospective case series involving patients with nAMD or DME reported a 3.7% incidence of intraocular inflammation per injection of aflibercept 8 mg. Reassuringly, all cases were mild and resolved with anti-inflammatory treatment without any loss of BCVA [45]. Pharmacovigilance analysis of the FDA Adverse Event Reporting System (FAERS) Database identified a possible increased risk of retinal vasculitis with aflibercept 8 mg compared with 2 mg, although it was noted that it was not possible to establish causal relationships between formulations and AEs based on these data [46].

While clinical trial data support the overall safety of aflibercept 8 mg, concerns remain about the relatively short follow-up period in the trials and the selective criteria for recruitment to the study [11, 12], which may therefore not fully represent real-world populations. These limitations highlight the importance of ongoing post-marketing surveillance [12, 47, 48]. Long-term real-world experience will be important, particularly with regards to monitoring any intraocular inflammation events and the potential implications related to the higher injection volume in susceptible eyes. Patients should be advised to promptly report symptoms such as inflammation, vision changes, or floaters for early detection of adverse events for intravitreal procedures in general, and clinicians should monitor patients carefully after administration [49, 50].

There is a need for careful monitoring of individual patients and general pharmacovigilance to build confidence in the use of aflibercept 8 mg, but it is important to note the robust evidence supporting the overall safety profile.

Clinical implications of the consensus

Here, we have reviewed the evidence for, and summarized our recommendations on, the use of aflibercept 8 mg in clinical practices. Aflibercept 8 mg represents a viable treatment option with an extended injection interval for patients with nAMD or DME, with the possibility of improving treatment adherence, and therefore outcomes. Although real-world data are limited [31], the expert panel discussed practical

considerations in Italy and offered evidence-based guidance of how to manage various clinical situations.

The application of any clinical guidance hinges on the capability of healthcare professionals in understanding the whys and hows of changing practice, the opportunity for such change to happen, as well as the motivation to modify existing practice and take up new habits [17]. These factors all substantially influence whether a clinical consensus can be translated to improved practice and patient outcomes. Therefore, we conducted a thorough behavioral analysis against some clinically pertinent statements to identify potential challenges that, if addressed, could facilitate the advancement of therapy. The COM-B model [16, 17] has been extensively applied in healthcare to structure intervention design and behavior analysis, and it is supported by over 750 scientific publications. Overall, we found an opportunity to expand the reach and reinforce education among healthcare professionals on novel therapies and treatment strategies (such as individualizing a T&E protocol), as well as the natural progressions of nAMD or DME. We also found substantial regulatory or organizational constraints, which may require additional evidence generation, and organizational, technological, or logistical support (e.g. remote monitoring or home OCT) to overcome. From a motivational perspective, clinicians may also benefit from knowledge and experience-sharing to gain confidence in counselling patients and applying novel treatments and treatment strategies in the real world. To address these challenges, we have provided recommendations (Fig. 1).

Recommendations:

- Strengthen clinical training programs to emphasize the importance of treatment extension in appropriate patients.
- Cultivate a sense of urgency among healthcare providers on the need for early diagnosis and treatment of nAMD to prevent irreversible loss of vision.
- Standardize treatment protocols to ensure consistent and effective care.
- Strengthen patient education to promote understanding and to improve adherence.
- Implement flexible T&E models supported by remote monitoring technologies such as home OCT to alleviate concerns of undertreatment.
- For at-risk patients, employ balanced communication strategies and establish rigorous monitoring protocols to ensure timely intervention.

Fig. 1 Strategies to address challenges in advancing the use of aflibercept 8 mg. nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; T&E, treat-and-extend

Our consensus is limited by the fact that all members of our expert panel are from Italy and, as such, may not fully reflect clinical situations in other parts of the world, including where biosimilars of aflibercept 2 mg or off-label bevacizumab may be required as first-line treatment. However, the panel represents varied healthcare facilities across urban and rural parts of Italy. Another limitation is that our focus is on the use of aflibercept 8 mg and we are unable to discuss in-depth aflibercept 8 mg in comparison with other anti-VEGFs. Nevertheless, our consensus is balanced by a key strength: the inclusion of behavioral analyses on the clinical applicability of our consensus statements. This uncovers potential barriers in applying our clinical recommendations in the real world and helps define targeted strategies to overcome them. The robustness of the development process of the consensus along with the use of a behavioral science framework provides comprehensive actions that can be taken to further optimize and address barriers to implementation in clinical practice.

Appendix 1: List of participants in Delphi consensus (Eight consensus group)

Teresio Avitabile	Department of Ophthalmology, University of Catania, Catania, Italy
Daniela Bacherini	Department of Neurosciences, Psychology, Drug Research, and Child Health, Eye Clinic, University of Florence, Azienda Ospedaliero Universitaria Careggi, Florence, Italy.
Francesco Boscia	Department of Translational Biomedicine Neuroscience, University of Bari "Aldo Moro", Bari, Italy
Flavia Chiosi	Department of Ophthalmology, Azienda Ospedaliera dei Colli-Ospedale Monaldi, Naples, Italy
Rodolfo Mastropasqua	Department of Neurosciences, Imaging and Clinical Sciences, University "G. d'Annunzio" Chieti-Pescara, Chieti, Italy
Angelo Minnella	Ophthalmology Unit, Fondazione Policlinico Universitario A. Gemelli- IRCCS, Largo F. Vito 1, Rome, Italy.
Francesco Parmeggiani	Department of Translational Medicine, University of Ferrara, Ferrara, Italy.
Maria Cristina Parravano	UniCamillus-Saint Camillus International University of Health Sciences, Rome, Italy.
Elisabetta Pilotto	Department of Ophthalmology, University of Padova, Padova, Italy.
Giuseppe Querques	Ophthalmology Unit – Policlinic of Modena, Department of Surgical, Medical, Dental and Morphological Sciences, Faculty of Medicine, UNIMORE, University of Modena and Reggio Emilia
Giovanni Staurengi	Eye Clinic, Department of Biomedical and Clinical Science, Luigi Sacco Hospital, University of Milan, Milan, Italy

Lisa Toto	Department of Neurosciences, Imaging and Clinical Sciences, University "G. d'Annunzio" Chieti-Pescara, Chieti, Italy
Maria Vadalà	Biomedicine, Neuroscience and Advance Diagnostic (BIND) Department, University of Palermo, Palermo, Italy.
Monica Varano	IRCCS-Fondazione Bietti, Rome, Italy
Daniele Veritti	Department of Ophthalmology-Medicine, University of Udine, Udine, Italy;
Francesco Viola	Ophthalmology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
Stela Vujosevic	Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy.

Appendix 2: List of members of the leading panel

Francesco Bandello	IRCCS San Raffaele Scientific Institute, Department of Ophthalmology, Milan, Italy
Enrico Borrelli	University of Turin, Department of Surgical Sciences, Turin, Italy; "City of Health and Sciences" Hospital, Department of Ophthalmology, Turin, Italy
Sandro De Falco	Institute of Genetics and Biophysics 'Adriano Buzzati-Traverso' – CNR, Angiogenesis Lab, Naples, Italy
Alessandro Invernizzi	Ospedale Luigi Sacco, Eye Clinic, Milan, Italy; University of Milan, Department of Biomedical and Clinical Sciences, Milan, Italy
Paolo Lanzetta	University of Udine, Department of Medicine - Ophthalmology, Udine, Italy; Istituto Europeo di Microchirurgia Oculare - IEMO, Udine, Italy
Marco Lupidi	Polytechnic University of Marche, Eye Clinic, Department of Experimental and Clinical Medicine, Ancona, Italy
Edoardo Midena	University of Padova, Department of Neuroscience-Ophthalmology, Padova, Italy
Federico Ricci	Tor Vergata University, Department of Experimental Medicine, Rome, Italy.

Appendix 3: List of participants in the workshop

Francesco Bandello	IRCCS San Raffaele Scientific Institute, Department of Ophthalmology, Milan, Italy
Francesco Boscia	Department of Translational Biomedicine Neuroscience, University of Bari "Aldo Moro", Bari, Italy
Giovanni Staurengi	Eye Clinic, Department of Biomedical and Clinical Science, Luigi Sacco Hospital, University of Milan, Milan, Italy
Maria Vadalà	Biomedicine, Neuroscience and Advance Diagnostic (BIND) Department, University of Palermo, Palermo, Italy.
Monica Varano	IRCCS-Fondazione Bietti, Rome, Italy

Daniele Veritti	Department of Ophthalmology-Medicine, University of Udine, Udine, Italy;
Francesco Viola	Ophthalmology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Poli- clinico, Milan, Italy

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00417-026-07470-3>.

Acknowledgements Writing and editorial support was provided by Annie Liu, Magdalene Chu and Ben Searle of The Bloc AMEA, and Karen Yee of ApotheCom, UK, and funded by Bayer AG in accordance with Good Publication Practice (GPP) standards (*Ann Intern Med* 2022;175:1298–1304).

Authors' contributions Study conceptualization: P.L. and S.D. Study design and methodology: F.B., E.B. and P.L. Preparation of material/data collection/provision of resources: All authors. Analysis and investigation: All authors. Manuscript development and writing – review and editing: All authors.

Funding The meetings were funded by Bayer AG, with support from The Bloc Milan. Writing and editorial support was provided by The Bloc AMEA and ApotheCom, UK, and funded by Bayer AG.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval Not required as this research did not involve human subjects or animals.

Competing interests **Francesco Bandello:** Consultant for Abbvie, Adverum Biotechnologies, Alimera, Apellis, Bayer, Boehringer Ingelheim, Breye Therapeutics Aps, Fidia Ssoft, Hoffmann-La Roche, Outlook Therapeutics, Novartis, NTC Pharma, Oxurion NV, 4D Molecular Therapeutics, SIFI. **Enrico Borrelli:** Member of the Editorial Board of Graefe's Archive for Clinical and Experimental Ophthalmology, not involved in peer review or editorial decisions for this manuscript. Funding from Bayer, Roche, Abbvie and Zeiss. **Sandro De Falco:** Consultant for Bayer. **Alessandro Invernizzi:** Consultant for Bayer, Novartis, Roche, AbbVie, Heidelberg Engineering. **Paolo Lanzetta:** Consultant for 4DMT, AbbVie, Adverum, Annexon, Apellis, Bausch & Lomb, Bayer, Biogen, Boehringer Ingelheim, Celltrion, EyePoint, I-Care, Genentech, MSD, Novartis, Ocular Therapeutix, Outlook Therapeutics, and Roche. **Marco Lupidi:** Financial interest in Abbvie, Bayer, Heidelberg Engineering, Roche. **Edoardo Midenà:** No competing interests. **Federico Ricci:** No competing interests.

References

- Almony A (2023) Treatment approaches for neovascular age-related macular degeneration and diabetic macular edema. *Am J Manag Care* 29:S81–S89. <https://doi.org/10.37765/ajmc.2023.89386>
- World Health Organisation (2026) Vision impairment and blindness. <https://www.who.int/news-room/fact-sheets/detail/blindness-and-visual-impairment>
- Wong WL, Su X, Li X, Cheung CMG, Klein R, Cheng C-Y, Wong TY (2014) Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *Lancet Global Health* 2:e106–e116. [https://doi.org/10.1016/S2214-109X\(13\)70145-1](https://doi.org/10.1016/S2214-109X(13)70145-1)
- Teo ZL, Tham Y-C, Yu M, Chee ML, Rim TH, Cheung N, Bikbov MM, Wang YX, Tang Y, Lu Y, Wong IY, Ting DSW, Tan GSW, Jonas JB, Sabanayagam C, Wong TY, Cheng C-Y (2021) Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. *Ophthalmology* 128:1580–1591. <https://doi.org/10.1016/j.ophtha.2021.04.027>
- Almony A (2023) Disease burden of neovascular age-related macular degeneration and diabetic macular edema. *Am J Manag Care* 29:S75–S80. <https://doi.org/10.37765/ajmc.2023.89387>
- European Medicines Agency (2026) Beovu (brolucizumab): European Public Assessment Report (EPAR) Product Information [accessed June 2026]
- Robinson K, Cooper SJ, Persaud S, Frederick JL, Singh RP (2025) Discordance among patients and ophthalmologists regarding the burden of intravitreal injections. *Clin Ophthalmol* 19:2637–2645. <https://doi.org/10.2147/OPTH.S532179>
- Reitan G, Kjelleveold Haugen IB, Andersen K, Bragadottir R, Bindesboll C (2023) Through the Eyes of Patients: Understanding Treatment Burden of Intravitreal Anti-VEGF Injections for nAMD Patients in Norway. *Clin Ophthalmol* 17:1465–1474. <https://doi.org/10.2147/OPTH.S409103>
- Sivaprasad S, Oyedunde S (2016) Impact of injection therapy on retinal patients with diabetic macular edema or retinal vein occlusion. *Clin Ophthalmol* 10:939–946. <https://doi.org/10.2147/OPTH.S100168>
- Wykoff CC, Brown DM, Reed K, Berliner AJ, Gerstenblith AT, Breazna A, Abraham P, Fein JG, Chu KW, Clark WL, Leal S, Schmelter T, Hirshberg B, Yancopoulos GD, Vitti R, CANDELA Study Investigators (2023) Effect of high-dose intravitreal aflibercept, 8 mg, in patients with neovascular age-related macular degeneration: the Phase 2 CANDELA randomized clinical trial. *JAMA Ophthalmol* 141:834–842. <https://doi.org/10.1001/jamaophthalmol.2023.2421>
- Brown DM, Boyer DS, Do DV, Wykoff CC, Sakamoto T, Win P, Joshi S, Salehi-Had H, Seres A, Berliner AJ, Leal S, Vitti R, Chu KW, Reed K, Rao R, Cheng Y, Sun W, Voronca D, Bhore R, Schmidt-Ott U, Schmelter T, Schulze A, Zhang X, Hirshberg B, Yancopoulos GD, Sivaprasad S, PHOTON Investigators (2024) Intravitreal aflibercept 8 mg in diabetic macular oedema (PHOTON): 48-week results from a randomised, double-masked, non-inferiority, phase 2/3 trial. *Lancet* 403:1153–1163. [https://doi.org/10.1016/S0140-6736\(23\)02577-1](https://doi.org/10.1016/S0140-6736(23)02577-1)
- Lanzetta P, Korobelnik J-F, Heier JS, Leal S, Holz FG, Clark WL, Eichenbaum D, Iida T, Xiaodong S, Berliner AJ, Schulze A, Schmelter T, Schmidt-Ott U, Zhang X, Vitti R, Chu KW, Reed K, Rao R, Bhore R, Cheng Y, Sun W, Hirshberg B, Yancopoulos GD, Wong TY (2024) Intravitreal aflibercept 8 mg in neovascular age-related macular degeneration (PULSAR): 48-week results from a randomised, double-masked, non-inferiority, phase 3 trial. *Lancet* 403:1141–1152. [https://doi.org/10.1016/S0140-6736\(24\)00063-1](https://doi.org/10.1016/S0140-6736(24)00063-1)
- Korobelnik J-F, Lanzetta P, Leal S, Holz FG, Clark WL, Eichenbaum D, Iida T, Sun X, Berliner AJ, Schulze A, Zhao M, Schmelter T, Schmidt-Ott U, Zhang X, Morgan-Warren P, Hasanbasic Z, Vitti R, Chu KW, Reed K, Bhore R, Cheng Y, Bai Z, Hirshberg B, Yancopoulos GD, Wong TY, PULSAR Investigators (2025) Intravitreal Aflibercept 8 mg in Neovascular Age-related Macular Degeneration: 96-Week Results from the Randomized Phase 3 PULSAR Trial. *Ophthalmology* S0161–6420012500532. <https://doi.org/10.1016/j.ophtha.2025.08.022>
- Veritti D, Sarao V, Lanzetta P (2025) Extended duration of VEGF inhibition with aflibercept 8 mg: the role of reduced ocular

- clearance. *Graefes Arch Clin Exp Ophthalmol*. <https://doi.org/10.1007/s00417-025-06847-0>
15. Nasa P, Jain R, Juneja D (2021) Delphi methodology in health-care research: How to decide its appropriateness. *World J Methodol* 11:116–129. <https://doi.org/10.5662/wjm.v11.i4.116>
 16. Cane J, O'Connor D, Michie S (2012) Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implement Sci* 7:37. <https://doi.org/10.1186/1748-5908-7-37>
 17. Michie S, van Stralen MM, West R (2011) The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 6:42. <https://doi.org/10.1186/1748-5908-6-42>
 18. Do DV, Wykoff CC, Sivaprasad S, Brown DM, Boyer DS, Sakamoto T, Win P, Joshi S, Salehi-Had H, Seres A, Berliner AJ, Leal S, Vitti R, Chu KW, Reed K, Cheng Y, Bhore R, Bai Z, Schmidt-Ott U, Schmelter T, Schulze A, Hasanbasic Z, Morgan-Warren PJ, Zhang X, Hirshberg B, Yancopoulos GD (2025) Intravitreal Afibercept 8 mg for Diabetic Macular Edema: Ninety-Six-Week Results from the Randomized Phase 2/3 PHOTON Trial. *Ophthalmol DOI*. <https://doi.org/10.1016/j.ophtha.2025.10.028>
 19. Payne CJ, Gupta U, Maatouk CM, Kuo BL, Perkins SW, Singh RP, Talcott KE (2024) Real-world effects of anti-vascular endothelial growth factor injection frequency on visual outcomes in patients with diabetic macular oedema. *Eye* 38:1687–1693. <https://doi.org/10.1038/s41433-024-02998-2>
 20. Khachigian LM, Liew G, Teo KYC, Wong TY, Mitchell P (2023) Emerging therapeutic strategies for unmet need in neovascular age-related macular degeneration. *J Transl Med* 21:133. <https://doi.org/10.1186/s12967-023-03937-7>
 21. Daien V, Finger RP, Talks JS, Mitchell P, Wong TY, Sakamoto T, Eldem BM, Korobelnik J-F (2021) Evolution of treatment paradigms in neovascular age-related macular degeneration: a review of real-world evidence. *Br J Ophthalmol* 105:1475–1479. <https://doi.org/10.1136/bjophthalmol-2020-317434>
 22. Chaikitmongkol V, Sagong M, Lai TYY, Tan GSW, Ngah NF, Ohji M, Mitchell P, Yang C-H, Ruamviboonsuk P, Wong I, Sakamoto T, Rajendran A, Chen Y, Lam DSC, Lai C-C, Wong TY, Cheung CMG, Chang A, Koh A (2021) Treat-and-extend regimens for the management of neovascular age-related macular degeneration and polypoidal choroidal vasculopathy: consensus and recommendations from the Asia-Pacific Vitreo-retina Society. *Asia Pac J Ophthalmol (Phila)* 10:507–518. <https://doi.org/10.1097/APO.0000000000000445>
 23. American Academy of Ophthalmology. Age-related macular degeneration preferred practice pattern 2026. <https://www.aao.org/education/preferred-practice-pattern/age-related-macular-degeneration-ppp>
 24. American Academy of Ophthalmology. Diabetic retinopathy preferred practice pattern 2024. <https://www.aao.org/education/preferred-practice-pattern/diabetic-retinopathy-ppp>
 25. Veritti D, Sarao V, Lanzetta P (2025) From pro-re-nata to fixed-interval regimen: evolving real-world treatment paradigms in anti-VEGF therapy for neovascular AMD. *Eye (Lond)* 39:1349–1355. <https://doi.org/10.1038/s41433-025-03627-2>
 26. Chaudhary V (2023) Treat & extend in neovascular age-related macular degeneration: how we got here and where do we go next? *Eye* 37:581–583. <https://doi.org/10.1038/s41433-022-02221-0>
 27. Gale R, Awad MH, Bailey C, Cackett P, Chhabra R, Downey L, Ghanchi F, Kotagiri A, Narendran N, Pearce I, Peto T, Sivaprasad S, Younis S, Napier J, Gilbert R, Ismat S (2026) Afibercept 8 mg treat-and-extend pathway for the treatment of neovascular age-related macular degeneration: guidance from a UK expert panel. *Eye (Lond)* 40:959–965. <https://doi.org/10.1038/s41433-025-04180-8>
 28. Shellvarajah M, Nguyen V, Steinmann S, Gillies MC, Sagkriotis A, Barthelmes D (2025) Adherence to anti-VEGF treatment in patients with neovascular age-related macular degeneration: a real-world study. *Ophthalmol Ther* 14:1261–1269. <https://doi.org/10.1007/s40123-025-01140-z>
 29. Iglicki M, Gonzalez DP, Loewenstein A, Zur D (2021) Longer-acting treatments for neovascular age-related macular degeneration-present and future. *Eye (Lond)* 35:1111–1116. <https://doi.org/10.1038/s41433-020-01309-9>
 30. The Royal College of Ophthalmologists (2024) Commissioning guidance. Age-related macular degeneration services: evidence base. <https://www.rcophth.ac.uk/wp-content/uploads/2021/08/A-MD-Commissioning-Guidance-Evidence-Base-2024.pdf>
 31. Kalavar M, Sridhar J (2025) Clinical trials and real-world studies examining faricimab and high-dose aflibercept for wet age-related macular degeneration and diabetic macular edema. *Curr Opin Ophthalmol* 36:189–198. <https://doi.org/10.1097/ICU.0000000000001129>
 32. Bouaziz M, Cheng T, Minuti A, Denisova K, Barmettler A (2022) Shared decision making in ophthalmology: a scoping review. *Am J Ophthalmol* 237:146–153. <https://doi.org/10.1016/j.ajo.2021.12.005>
 33. Rittiphairoj T, Mir TA, Li T, Virgili G (2020) Intravitreal steroids for macular edema in diabetes. *Cochrane Database Syst Rev* 11:CD005656. <https://doi.org/10.1002/14651858.CD005656.pub3>
 34. Zafar S, Walder A, Virani S, Biggerstaff K, Orenge-Nania S, Chang J, Channa R (2023) Systemic adverse events among patients with diabetes treated with intravitreal anti-vascular endothelial growth factor injections. *JAMA Ophthalmol* 141:658–666. <https://doi.org/10.1001/jamaophthalmol.2023.2098>
 35. Korobelnik J-F, Lanzetta P, Wykoff CC, Wong TY, Zhang X, Morgan-Warren P, Fitzpatrick S, Leal S, Brunck L, Hasanbasic Z, Chu KW, Reed K, Sivaprasad S (2024) Sustained disease control with aflibercept 8 mg: a new benchmark in the management of retinal neovascular diseases. *Eye* 38:3218–3221. <https://doi.org/10.1038/s41433-024-03312-w>
 36. Giocanti-Aurégan A, Garcia-Layana A, Peto T, Gentile B, Chi GC, Mirt M, Kosmas CE, Lambert J, Lanar S, Lewis HB, Holekamp NM (2022) Drivers of and barriers to adherence to neovascular age-related macular degeneration and diabetic macular edema treatment management plans: a multi-national qualitative study. *Patient Prefer Adherence* 16:587–604. <https://doi.org/10.2147/PPA.S347713>
 37. Wykoff CC, Clark WL, Nielsen JS, Brill JV, Greene LS, Hegen CL (2018) Optimizing anti-VEGF treatment outcomes for patients with Neovascular age-related macular degeneration. *J Manag Care Spec Pharm* 24 (Number 2-a Suppl). <https://doi.org/10.18553/jmcp.2018.24.2-a.s3>
 38. Chakravarthy U, Pillai N, Syntosi A, Barclay L, Best C, Sagkriotis A (2020) Association between visual acuity, lesion activity markers and retreatment decisions in neovascular age-related macular degeneration. *Eye* 34:2249–2256. <https://doi.org/10.1038/s41433-020-0799-y>
 39. Chakravarthy U, Havilio M, Syntosi A, Pillai N, Wilkes E, Benyamini G, Best C, Sagkriotis A (2021) Impact of macular fluid volume fluctuations on visual acuity during anti-VEGF therapy in eyes with nAMD. *Eye (Lond)* 35:2983–2990. <https://doi.org/10.1038/s41433-020-01354-4>
 40. Wojciechowski P, Wdowiak M, Panek M, Lunk I, Carrasco J, Zhang X, Wu O, Korobelnik J-F, Lanzetta P (2025) Efficacy, safety, and injection frequency with novel aflibercept 8 mg in neovascular age-related macular degeneration: a comparison with existing anti-VEGF regimens using a Bayesian network meta-analysis. *Ophthalmol Ther* 14:733–753. <https://doi.org/10.1007/s40123-025-01098-y>
 41. Sarao V, Veritti D, Bonini F, Martin AA, Lanzetta P (2025) Early intraocular pressure dynamics following aflibercept 8 mg

- versus aflibercept 2 mg: a propensity score-matched analysis. *Eye* 39:1933–1939. <https://doi.org/10.1038/s41433-025-03765-7>
42. Paris A, Volpe G, Perruchoud-Ader K, Casanova A, Menghini M, Grimaldi G (2024) Short-term intraocular pressure changes after intravitreal aflibercept 2 mg, aflibercept 8 mg and faricimab: a prospective, comparative study. *Br J Ophthalmol*. <https://doi.org/10.1136/bjo-2024-326053>
 43. Liu Y, Wang T, Zhang X, Li M, Han L, Lan X, Wang L, Wang X (2025) Contributing factors to short-term intraocular pressure elevation following intravitreal anti-VEGF injections. *BMC Ophthalmol* 25:281. <https://doi.org/10.1186/s12886-025-04111-x>
 44. Zaman M, Alowedi S, Sharma S (2025) Anterior chamber paracentesis for increased intraocular pressure with intravitreal injections: systematic review and meta-analysis. *Can J Ophthalmol* 60:e934–e945. <https://doi.org/10.1016/j.jejo.2025.06.003>
 45. Binder KE, Bleidißel N, Charbel Issa P, Maier M, Coulibaly LM (2025) Noninfectious Intraocular Inflammation After Intravitreal Aflibercept. *JAMA Ophthalmol* 143:499–506. <https://doi.org/10.1001/jamaophthalmol.2025.0969>
 46. Prasad M, Ramsey DJ (2026) Adverse events reported with standard-dose and high-dose aflibercept: a FAERS pharmacovigilance study. *Vision (Basel)*. <https://doi.org/10.3390/vision10020018>
 47. Musadiq M, Musadiq M, Latif F, Ng B, Azzopardi M, Gilead N, Needham A, Chong YJ (2025) Early real-world outcomes of switching to 8 mg aflibercept for neovascular age-related macular degeneration in the United Kingdom. *Life* 15:903. <https://doi.org/10.3390/life15060903>
 48. Cattaneo J, De Oliveira Figueiredo EC, Montesil A, Vermeirsch S, Eandi CM (2025) Early real-world outcomes of intravitreal aflibercept 8 mg in treatment-naïve neovascular AMD: AI-assisted fluid volume analysis. *Int J Retina Vitreous* 11:42. <https://doi.org/10.1186/s40942-025-00665-6>
 49. Santorsola M, Capuzzo M, Nasti G, Sabbatino F, Di Mauro A, Di Mauro G, Vanni G, Maiolino P, Correr M, Granata V, Gualillo O, Berretta M, Ottaiano A (2024) Exploring the spectrum of VEGF inhibitors' toxicities from systemic to intravitreal usage in medical practice. *Cancers* 16:350. <https://doi.org/10.3390/cancers16020350>
 50. Lam LA, Mehta S, Lad EM, Emerson GG, Jumper JM, Awh CC, Task Force on Intravitreal Injection Supplemental S (2021) Intravitreal injection therapy: current techniques and supplemental services. *J Vitreoretin Dis* 5:438–447. <https://doi.org/10.1177/24741264211028441>
 51. Oxford Centre of Evidence-Based Medicine. OCEBM levels of evidence. <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebml-levels-of-evidence>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

Authors and Affiliations

Francesco Bandello¹  · Enrico Borrelli^{2,3} · Sandro De Falco⁴ · Alessandro Invernizzi^{5,6} · Paolo Lanzetta^{7,8} · Marco Lupidi⁹ · Edoardo Midena¹⁰ · Federico Ricci¹¹ · on behalf of the Eight Consensus Group

✉ Francesco Bandello
bandello.francesco@hsr.it

¹ Department of Ophthalmology, IRCCS San Raffaele Scientific Institute, Milan, Italy

² Department of Surgical Sciences, University of Turin, Turin, Italy

³ Department of Ophthalmology, “City of Health and Sciences” Hospital, Turin, Italy

⁴ Angiogenesis Laboratory, Institute of Genetics and Biophysics ‘Adriano Buzzati-Traverso’ – CNR, Naples, Italy

⁵ Eye Clinic, Ospedale Luigi Sacco, Milan, Italy

⁶ Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy

⁷ Department of Medicine - Ophthalmology, University of Udine, Udine, Italy

⁸ Istituto Europeo di Microchirurgia Oculare - IEMO, Udine, Italy

⁹ Eye Clinic, Department of Experimental and Clinical Medicine, Polytechnic University of Marche, Ancona, Italy

¹⁰ Department of Neuroscience-Ophthalmology, University of Padova, Padova, Italy

¹¹ Department of Experimental Medicine, Tor Vergata University, Rome, Italy