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EURETINA EDUCATION PLATFORM

EURETINA CLINICAL TRENDS SERIES

Wet AMD & DME

by Prof. Sandrine Zweifel, MD, PhD

Neovascular Age-Related Macular Degeneration (nAMD) and Diabetic Macular Edema (DME)

In the inaugural edition of the EURETINA Clinical Trends Series, Prof. Sandrine Zweifel, member of the EURETINA AMD Subspecialty Section provides insights on findings from the 2024 EURETINA Clinical Trends Survey, offering a detailed look at how members approach nAMD and DME diagnosis and management. She also shares her perspective on how she addresses these conditions in her practice and how trends in the survey data align with the broader landscape of global retina care.

Diagnosis and monitoring of nAMD and DME

According to 2024 EURETINA Clinical Trends Survey OCT is the most commonly used tool for diagnosis and monitoring both nAMD (**Figure 1**) and DME (**Figure 2**). While OCT remains the cornerstone, the value of a multimodal imaging approach cannot be overstated, especially in cases where patients are not responding well to treatment. In my clinical practice, when there is suboptimal response to anti-VEGF therapy, I routinely recommend additional imaging modalities to gain a more comprehensive understanding of the underlying pathology.

At the diagnostic stage, multimodal imaging can help confirm the presence of macular neovascularization (MNV) and rule out alternative diagnoses. For example, fundus autofluorescence is useful for identifying inherited retinal diseases that may mimic AMD, while FA and indocyanine ICG can help visualize lesion type and rule out other conditions.

During follow-up, especially when the patient deviates from the expected treatment trajectory, these tools continue to play a critical role. Revisiting FA/ICG can uncover conditions such as aneurysmal type 1 MNV or so called polypoidal choroidal vasculopathy or type 3 MNV/retinal angiomatous proliferation, which may respond differently to standard therapy and require tailored management strategies. Ultimately, multimodal imaging enables more precise diagnosis and helps guide individualized treatment decisions, both at baseline and throughout the disease course.

Peripheral evaluation matters in diabetic retinopathy, widefield FA findings correlate with worse visual prognosis as has been shown by the DRCR Retina Network. And the timing when to perform FA is important as well, ideally, widefield FA should be either performed prior to anti-VEGF therapy, after stopping injections, or at least 4-6 weeks after an injection if the patient continues with anti-VEGF injections.

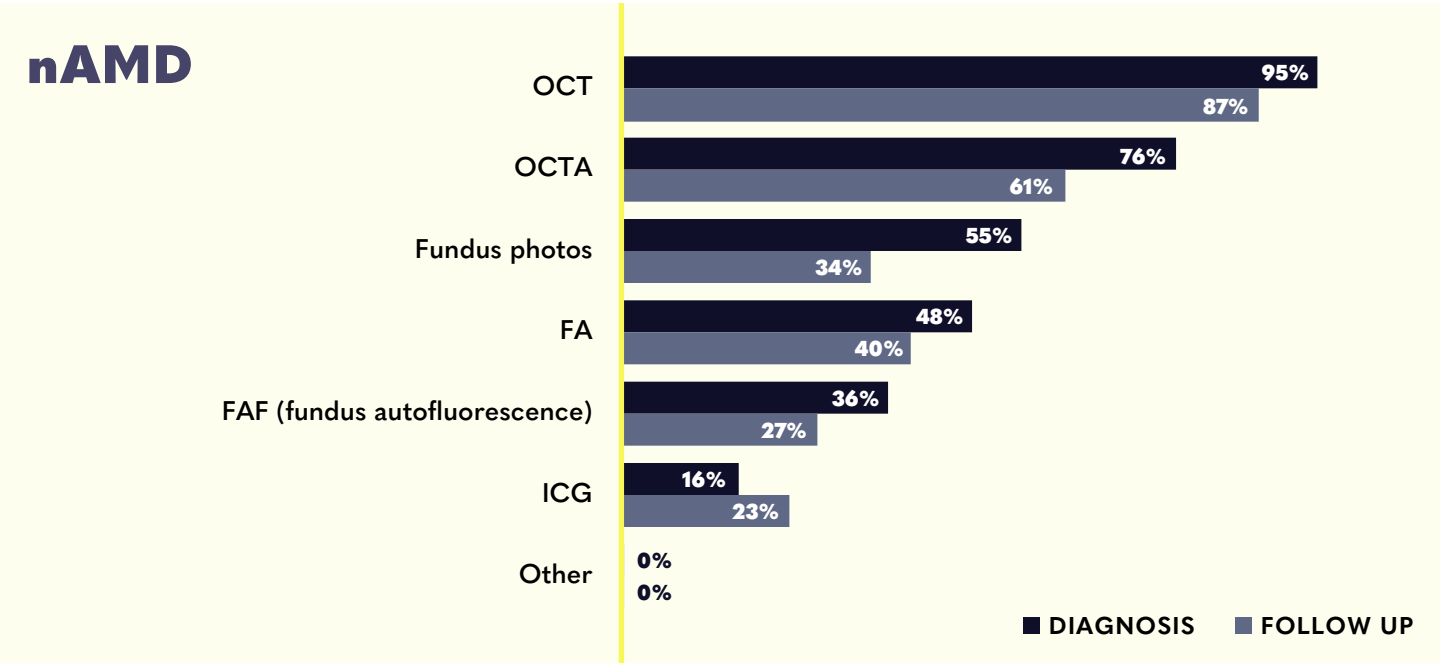

FIGURE 1. *What are all the imaging/diagnostic techniques that you use at the time of diagnosis vs follow-up for a patient who is NOT responding well to treatment for nAMD patients? (Select all that apply.)*

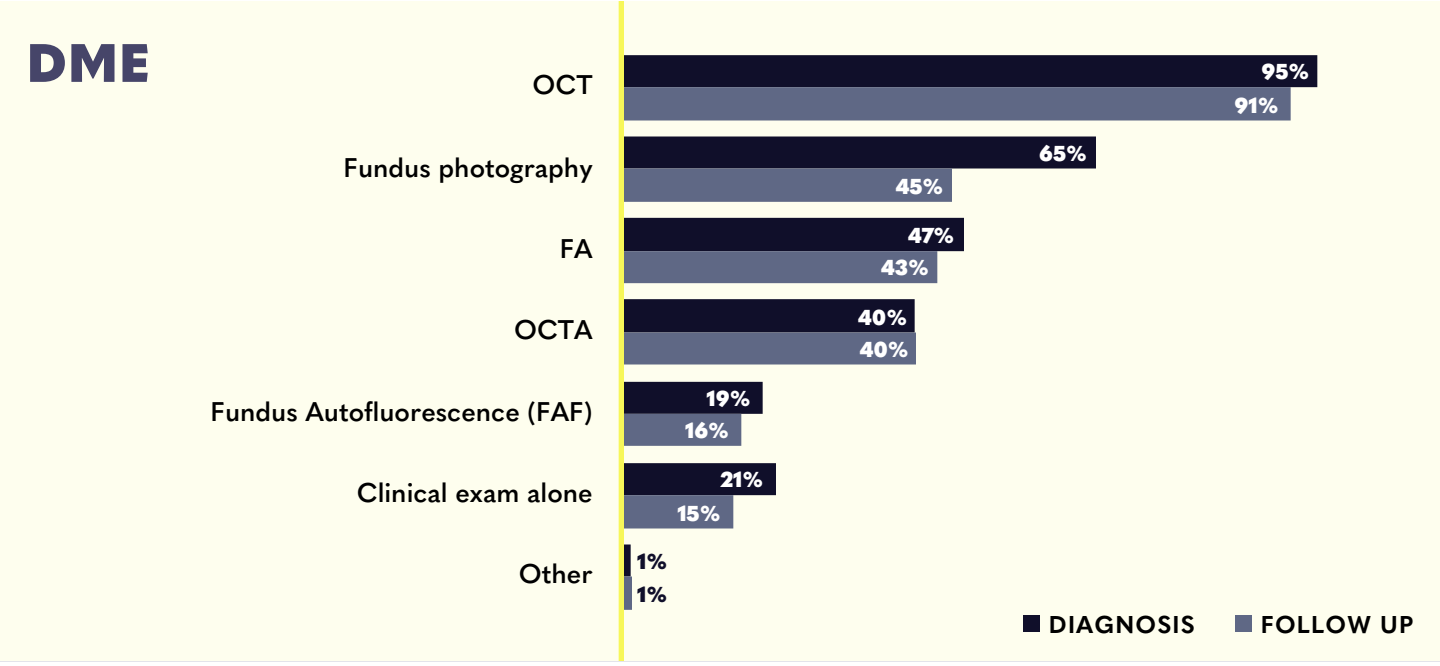

FIGURE 2. *What are all the imaging/diagnostic techniques that you use at the time of diagnosis vs follow-up for a patient who is NOT responding well to treatment for DME patients? (Select all that apply.)*

Anti-VEGF Therapy

Note: *Both nAMD and DME are commonly treated with anti-VEGF therapies, which inhibit vascular endothelial growth factor to reduce abnormal blood vessel growth and vascular leakage in the retina. In this section, we'll explore the initiation of anti-VEGF therapy, considerations for switching agents, and key unmet needs. While recognizing the clinical nuances of each disease, we will move fluidly between nAMD and DME to highlight both shared challenges and distinct treatment dynamics.*

INITIATING TREATMENT

The top three factors used to decide when to initiate anti-VEGF therapy for nAMD are the development of subretinal fluid (SRF) and/or intraretinal fluid (IRF) on OCT, fluid and/or heme in clinical exam, and the development of subRPE fluid on OCT, according to survey respondents (**Figure 3**).

I largely agree with these responses, as findings on OCT and clinical exam are well-established markers of active disease and have been closely associated with the risk of irreversible vision loss if left untreated. I would add, however, that increasing pigment epithelial detachment (PED), even in the absence of SRF or IRF, can also serve as a treatment criterion for patients with neovascular AMD in my practice. While PED alone may not always indicate active exudation, a growing fibrovascular PED can suggest evolving disease activity and may justify early intervention to prevent further progression.

Conversely, the presence of MNV without fluid—referred to as non-exudative or subclinical MNV—is not currently considered an indication for treatment. This view is supported by recent evidence from two large prospective randomized trials, PREVENT[1] and PRO-CON[2], which explored prophylactic anti-VEGF treatment in these cases. Neither study demonstrated significant benefit in terms of visual outcomes or conversion rates to exudative disease, reinforcing the rationale for a more conservative, observation-based approach in non-exudative MNV.

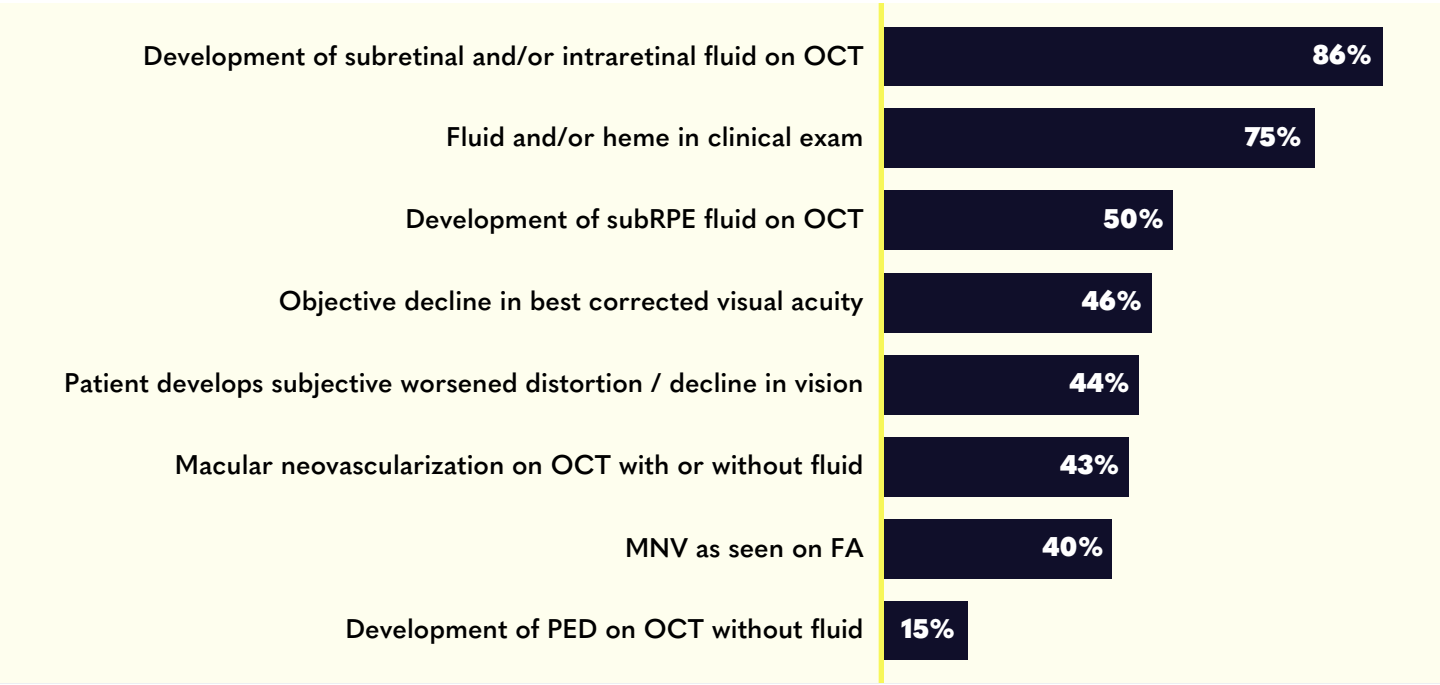

FIGURE 3. ***When do you decide to initiate anti-VEGF therapy in a patient with nAMD? (Select all that apply.)***

SWITCHING TREATMENTS

Deciding when to switch therapies in DME patients who are not responding optimally to anti-VEGF treatment is a nuanced clinical judgment that involves balancing potential gains against the risks of premature change. Among respondents to the EURETINA Clinical Trends Survey, 73% of respondents switch after 3-5 injections (**Figure 4**).

There is evidence suggesting that some patients may continue to show incremental improvement if therapy is maintained consistently, and switching too early may forgo these benefits. In this context, a decision to persist with treatment may be justified if there are any signs of slow but ongoing response.

However, prolonging an ineffective regimen can also delay vision recovery, increase treatment burden, and strain healthcare resources. From a cost-benefit standpoint, the analysis often depends heavily on the reimbursement landscape and healthcare infrastructure of the treating country. In systems with strict cost controls or limited access to alternative therapies, a more conservative approach may prevail, whereas systems that support flexible treatment algorithms may permit earlier switches.

Supporting this perspective, post hoc analyses such as the ARIES and HARBOR substudies have modeled the impact of hypothetical treatment switches and found variable outcomes.[3,4] These findings underscore the need for individualized patient assessment and careful monitoring before making decisions about switching therapy. Ultimately, the goal is to avoid both premature and overly delayed changes, striking a balance that optimizes visual outcomes while maintaining cost-effectiveness and patient adherence.

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>
> *– Prof. Sandrine Zweifel, MD, PhD*

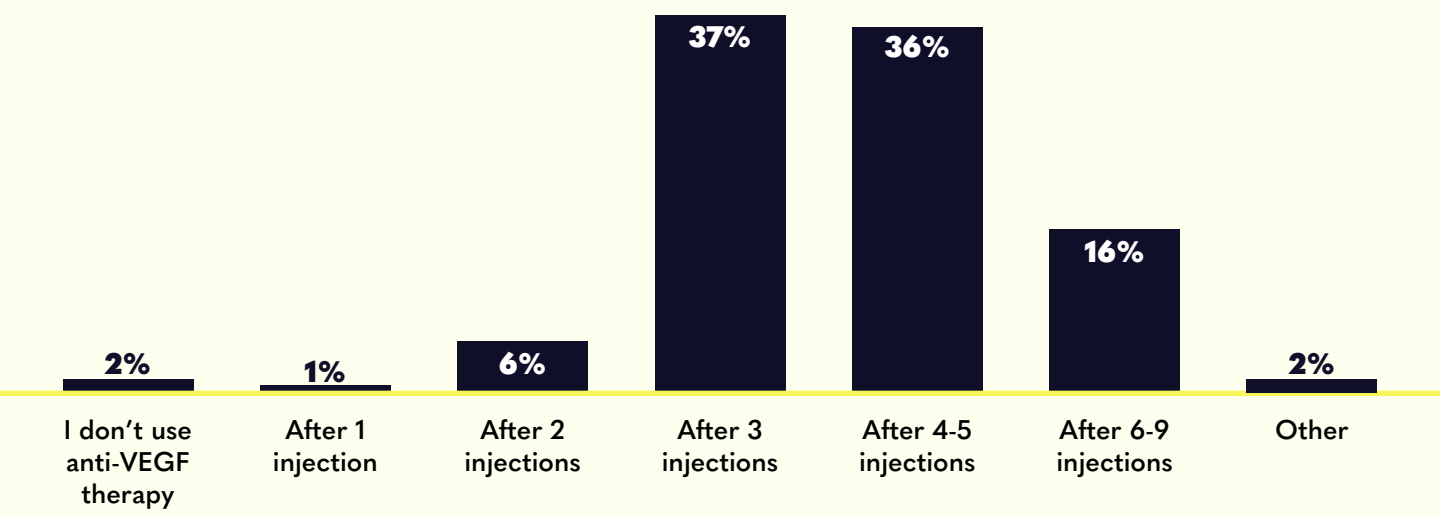

FIGURE 4. ***For your DME patients who are not responsive to primary anti-VEGF therapy, after how many injections do you consider an alternative?***

UNMET NEEDS FOR ANTI-VEGF TREATMENT

According to 2024 EURETINA Clinical Trends Survey respondents, the top three unmet needs for current anti-VEGF treatments were quantity of injections/ treatment burden for patients, need for extended duration of action, and improved functional outcomes/best-correct visual acuity as the most pressing unmet needs in current anti-VEGF therapy (**Figure 5**). Notably, the first two are closely linked: by extending the duration of action, we can naturally reduce the number of injections and clinic visits, which in turn alleviates the overall treatment burden for patients. This remains a major concern, particularly for elderly patients or those with limited access to care.

As for the need to improve functional outcomes, a key challenge lies in our inability to effectively address subretinal fibrosis, which continues to limit long-term visual potential even when fluid is well-controlled. Atrophy, which can be present even in the setting of fibrosis, presents another hurdle. Although we now have the first approved treatments for geographic atrophy, they are not yet approved or reimbursed in many parts of Europe, and the clinical benefit remains modest. Addressing these structural degenerative changes is critical if we are to move beyond stabilization and toward meaningful visual improvement for our patients.

The variability in visual and anatomic outcomes six months after initial anti-VEGF therapy for nAMD is influenced by several well-established clinical factors. As highlighted in previous discussions, one of the most important is the type of MNV, as classified by the CONAN criteria. Numerous studies, including our own work, have demonstrated that lesion subtype significantly correlates with prognosis.

A nuanced interpretation of retinal fluid characteristics is also essential. The presence and type of fluid—particularly subretinal versus intraretinal—often reflect underlying lesion subtype and can guide both initial treatment choice and ongoing management. For example, Type 1 MNV is more frequently associated with subretinal fluid, which may carry a more favorable visual prognosis compared to intraretinal fluid.

Beyond lesion type and fluid morphology, other baseline characteristics—such as starting visual acuity,

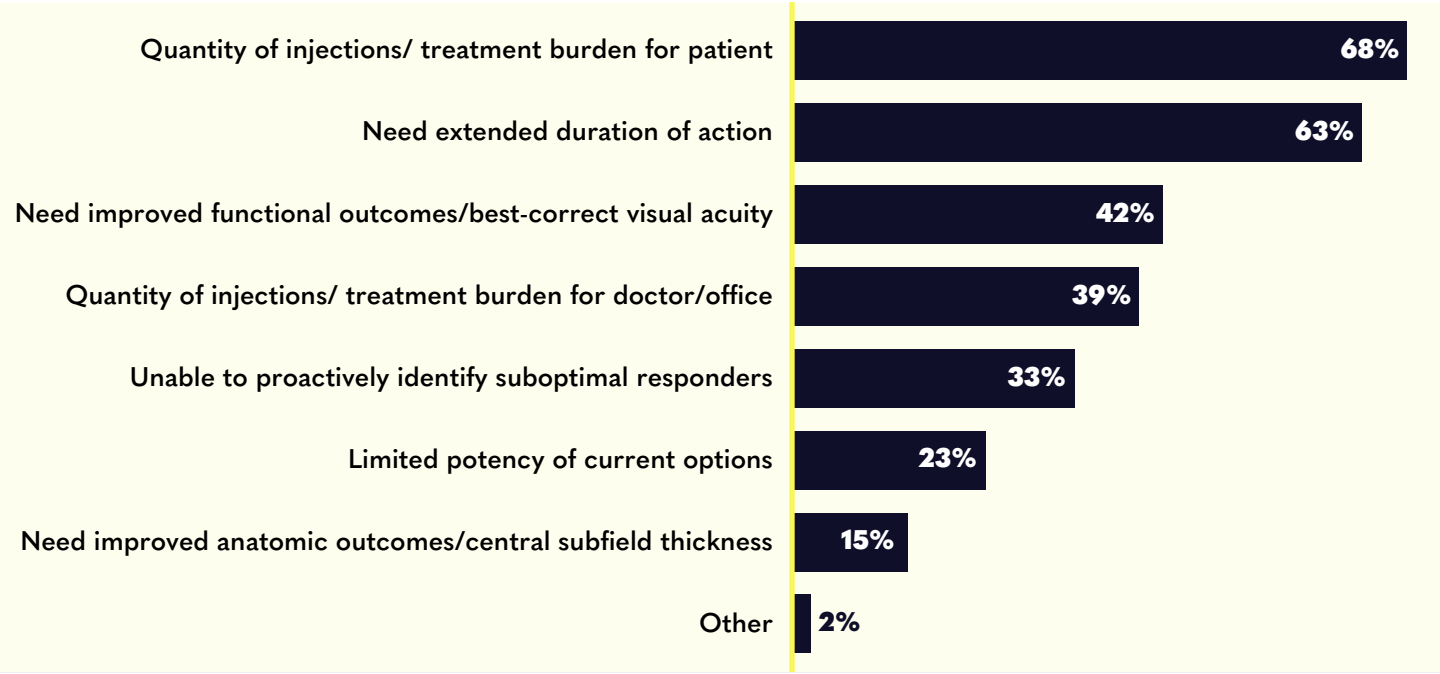

***FIGURE 5.** What is the largest unmet need for current anti-VEGF treatments? (Select up to 3 of the following.)*

the presence of macular atrophy or fibrosis, and lesion size—play key roles in determining treatment response. Additionally, patient adherence to follow-up and treatment schedules can significantly influence outcomes. When these clinical factors are integrated into treatment planning, they support a more personalized approach to nAMD care, helping to set realistic expectations and optimize visual results.

ADHERENCE TO TREATMENT

The survey explored reasons for treatment non-adherence and found broadly similar themes across both nAMD and DME. However, the frequency of clinic visits was cited as a barrier at a significantly higher rate for DME patients compared to those with nAMD (**Figure 6**).

In my experience, adherence patterns differ notably between patients with DME and those with nAMD, primarily due to differences in lifestyle and health burden. DME patients often fall within the working-age population and tend to juggle multiple healthcare responsibilities related to their diabetes. Many already have frequent appointments with endocrinologists, primary care providers, and other specialists, which can make it difficult to prioritize and consistently attend ophthalmic visits. As a result, non-adherence in this group is often tied to logistical challenges and competing medical demands.

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– Prof. Sandrine Zweifel, MD, PhD

In contrast, my nAMD patients are generally older and retired, which allows them to be more consistent with their eye care schedules. When these patients miss a visit, it is typically for acute or serious reasons—such as hospitalization, illness, or other emergent health issues—rather than due to time constraints or conflicting medical priorities.

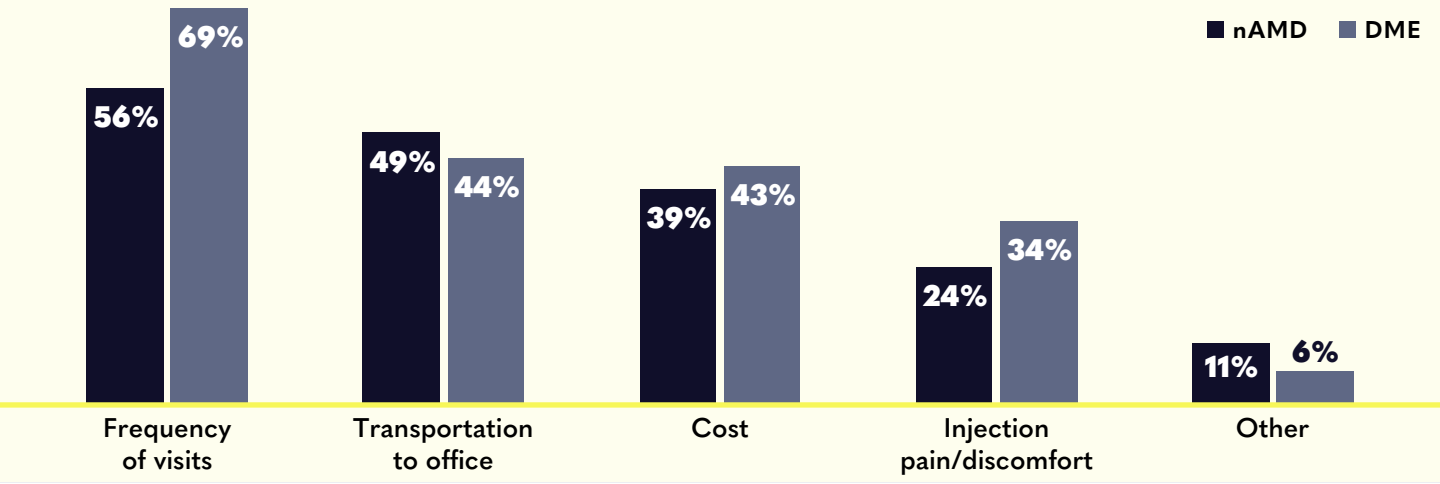

FIGURE 6. ***Of your nAMD/DME patients that do not adhere to their treatment regimen, what are their reasons for not adhering? (Select all that apply.)***

FURTHER INSIGHTS

Among survey respondents:

80%
use a treat and extend (T&E) or hybrid of T&E and PRN regimen for anti-VEGF injections for nAMD

48%
of nAMD patients are dry 6 months after their initial first-line treatment

15%
genetic test their patients for AMD

71%
see their DME patients every 1-3 months

41%
of DME patients have a CFT <250 microns after first line treatment

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3. Tuerksever C, Somfai GM, Oesch S, Machewitz T, Hasler PW, Zweifel S. Hypothetical Switch of Anti-Vascular Endothelial Growth Factor in Neovascular Age-Related Macular Degeneration: An ARIES Post Hoc Analysis. Ophthalmol Ther. 2022 Apr;11(2):613-627. doi: 10.1007/s40123-021-00448-w. Epub 2022 Jan 23. PMID: 35066801; PMCID: PMC8784022.

4. Zarbin M, Tsuboi M, Hill LF, Stoilov I. Simulating an Anti-Vascular Endothelial Growth Factor Switch in Neovascular Age-Related Macular Degeneration: A HARBOR Subanalysis. Ophthalmology. 2019 Jun;126(6):849-855. doi: 10.1016/j.ophtha.2019.01.003. Epub 2019 Jan 11. PMID: 30641096.

Notes

About the 2024 EURETINA Clinical Trends Survey

This report contains results of the 2024 EURETINA Clinical Trends Survey, conducted online in conjunction with the 24th Congress of EURETINA in Barcelona. Questions addressed several areas of clinical practice, including retinal diagnostics, AMD, DME, retinal detachment, myopia management, and gene therapy.

Over 3,000 physicians responded to the 131 questions, which were developed and reviewed with the EURETINA leadership and substantiated by a data scientist. To better identify the educational needs of its members, EURETINA leadership refers to the results of these annual surveys and the feedback they elicit. The collected data will also enhance the opportunities featured at the EURETINA Annual Congress and other educational channels such as the EURETINA Online Education Platform (IME ePlatform) as well as print and digital supplements.

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This year marks the 8th launch of the EURETINA Clinical Trends Survey. The survey's goal is to collect answers to key questions related to clinical opinions and practice patterns. Participate in this comprehensive survey and help us obtain responses from a significant percentage of doctors. The results will be reviewed by the EURETINA leadership and published in a supplement similar to the one you hold in your hand.

The survey can be taken online and in less than 15 minutes, you will make a meaningful contribution. In return, we will enter you in a draw for free 2026 delegate registration to the EURETINA annual congress.

Please click here or scan the QR code below to start the EURETINA 2025 Clinical Trends Survey:

Meet the Author

Prof. Sandrine Zweifel, MD, PhD

Prof. Sandrine Zweifel (MD, PhD) is a retina specialist, vice chair and head of the medical retina and imaging unit at the Department of Ophthalmology at the University Hospital Zurich, Switzerland. After her specialty training in Switzerland, Sandrine Zweifel did a clinical and research fellowship under the mentorship of K. Bailey Freund, Richard F. Spaide and Lawrence Yannuzzi in New York.

She was awarded the title of "Godmother of the Association of DMLA (AMD)" in 2011 and was appointed visiting professor at the Université Paris-Est Créteil Val de Marne in 2013. She received her "venia legend" in ophthalmology, in particular retinal diseases from the University of Zurich in 2014.

As head of the medical retina unit at the Department of Ophthalmology, Dr. Zweifel is responsible for the management of the medical retina and injection clinics, cataract service of patients with retinal diseases and is involved in training of medical students and registrars in ophthalmology.

The major research interest of Dr. Zweifel is retinal imaging, which is essential to the diagnosis, treatment, and long-term monitoring of both ocular diseases as well as systemic diseases with ocular manifestations. She has received awards for her contributions to scientific research and serves as a reviewer for many international journals. She has participated in numerous international randomized multicenter (phase II and III) clinical trials and authored numerous papers published in major international ophthalmology journals and book chapters. She has supervised numerous thesis in Medical School graduation and Specialization in Ophthalmology. Further, Dr. Zweifel has received grants from different foundations for her outstanding clinical research.

Dr. Zweifel is a member in different national and international ophthalmological societies, including the Swiss Vitreoretinal Group, Euretina, the Macula Society the American Academy of Ophthalmology, the Club Jules Gonin, the Association for Research in Vision and Ophthalmology and EVICR.net. She participates in numerous national and international meetings, with multiple invited speaker appointments.

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