



VISION ACADEMY VIEWPOINT

The Vision Academy is a partnership between Bayer and ophthalmic specialists, established with the aim of addressing key unmet needs in the field of retinal diseases: www.visionacademy.org.

Fundamental Principles of an Anti-VEGF Treatment Regimen

Background

Intravitreal anti-VEGF therapy is now considered the standard of care in the treatment of various retinal disorders. As therapy has evolved, so too have the treatment regimens employed by physicians in clinical practice; visual outcomes observed in the real world, however, have typically not reflected those reported in clinical trials. There are several possible reasons for this, including a lack of consensus on how best to administer anti-VEGF therapy and what should be the aims of treatment.

The Vision Academy Steering Committee agreed upon a series of fundamental principles of an anti-VEGF treatment regimen, using evidence from the literature to substantiate each point. Literature searches were performed using the MEDLINE/PubMed database (cut-off date: March 2016).

Endorsed by the Vision Academy in September 2016.





Viewpoint

Four principles were identified that are fundamental to any treatment regimen for anti-VEGF management of retinal diseases:

1. Maximize and maintain visual acuity (VA) benefits for all patients¹⁻⁷

- This should be the aim of anti-VEGF treatment for all patients, not just those who respond well to therapy
- Early initiation of therapy and a sufficient frequency of injections are both essential for maximizing and maintaining gains in visual acuity

2. Decide when to treat next, rather than whether to treat now 5,8-10

- Success of anti-VEGF treatment depends not only on the treatment of active disease but also on the prevention of disease recurrence and/or worsening
- Planning the date of the next anti-VEGF treatment helps to minimize the possibility of delays in treatment, allows time where needed for treatment approval to be obtained, and facilitates clinic management. Patients may also benefit from being able to plan for their next injection in good time
- A proactive treatment approach allows physicians to stay ahead
 of the disease and, by minimizing the need for intervening visits,
 helps to ease the burden on clinics and patients

3. Titrate the treatment intervals to match patients' needs¹⁰⁻¹⁵

- The duration of VEGF suppression varies between patients and differs between anti-VEGF agents
- Anti-VEGF agents with greater durations of action allow for longer extension of treatment intervals than for those with short durabilities
- Customization of the treatment interval to the individual patient removes the need for interim monitoring, while achieving optimal outcomes for the patient

4. Treat at each monitoring visit

- Monitoring and treating within the same appointment helps to eliminate the possibility of disease resurgence that can occur between separate monitoring and treatment appointments
- The number of appointments per patient is reduced, helping to ease clinic flow and patient burden

References

- Brown DM. Heier, et al. Intravitreal aflibercent injection for macular edema secondary to central retinal vein occlusion: 1-year results from the phase 3 COPERNICUS study. Am J Ophthalmol 2013; 155 (3): 429-437 e7.
- Korobelnik J-F, Holz FG, Roider J, et al. Intravitreal aflibercept injection for macular edema resulting from central retinal vein occlusion: One-year results of the phase 3 GALILEO study. Ophthalmology 2014; 121 (1): 202-208.
- Bayer plc. EYLEA 40 mg/mL solution for injection in a vial summary of product characteristics. Bayer plc; Newbury, Berkshire, UK, August 2016.
- 4. Holz FG, Tadayoni R, Beatty S, et al. Multi-country real-life experience of anti-vascular endothelial growth factor therapy for wet age-related macular degeneration. Br J Ophthalmol 2015; 99 (2): 220-226.
- 5. Oubraham H, Cohen SY, Samimi S, et al. Inject and extend dosing versus dosing as needed: A comparative retrospective study of ranibizumab in exudative age-related macular degeneration. Retina 2011; 31 (1): 26-30.
- Diabetic Retinopathy Clinical Research Network, Wells JA, Glassman AR et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. N Engl J Med 2015; 372 (13):
- 7. Lim JH, Wickremasinghe SS, Xie J, et al. Delay to treatment and visual outcomes in patients treated with antivascular endothelial growth factor for age-related macular degeneration. Am J Ophthalmol 2012; 153 (4): 678-686.
- 8. Hatz K and Prünte C. Changing from a pro re nata treatment regimen to a treat and extend regimen with ranibizumab in neovascular age-related macular degeneration. Br J Ophthalmol 2016; 100 (10): 1341-1345.
- Epstein D and Amrén U. Near vision outcome in patients with age-related macular degeneration treated with aflibercept. Retina 2016: 36 (9): 1773-1777.
- 10. Regillo CD. Prospective, multicenter investigation of aflibercept treat and extend therapy for neovascular agerelated macular degeneration (ATLAS Study): Two year results. Paper presented at the American Academy of Ophthalmology (AAO) 2015 Annual Meeting; Las Vegas, NV, USA, November 14-17, 2015.
- 11. Muether PS, Hermann MM, Dröge K et al. Long-term stability of vascular endothelial growth factor suppression time under ranibizumab treatment in age-related macular degeneration. Am J Ophthalmol 2013; 156 (5): 989-993 e2.
- 12. Fauser S. Schwabecker V and Muether PS. Suppression of intraocular vascular endothelial growth factor during aflibercept treatment of age-related macular degeneration. Am J Ophthalmol 2014; 158 (3): 532-536.
- 13. Muether PS. Droege KM and Fauser S. Vascular endothelial growth factor suppression times in patients with diabetic macular oedema treated with ranibizumab. Br J Ophthalmol 2014; 98 (2): 179-181.
- 14. Berg K, Hadzalic E, Gjertsen I, et al. Ranibizumab or bevacizumab for neovascular age-related macular degeneration according to the Lucentis compared to Avastin study treat-andextend protocol: Two-year results. Ophthalmology 2016; 123 (1):
- 15. Richard G, Monés J, Wolf S, et al. Scheduled versus pro re nata dosing in the VIEW trials. Ophthalmology 2015; 122 (12): 2497-2503.
- 16. Freund KB, Mrejen S and Gallego-Pinazo R. An update on the pharmacotherapy of neovascular age-related macular degeneration. Expert Opin Pharmacother 2013; 14 (8): 1017-
- 17. Engelbert M, Zweifel SA and Freund KB. "Treat and extend" dosing of intravitreal antivascular endothelial growth factor therapy for type 3 neovascularization/retinal angiomatous proliferation. Retina 2009; 29 (10): 1424-1431.

Further considerations

The four fundamental principles of a treatment regimen advocate use of a predictable, proactive and manageable treatment regimen in the clinic, with consideration of individual patient needs and elimination of delays in treatment. 16,17



If adopted in clinical practice, the four principles are anticipated to lead to benefits for both patient and physician, with improvements in organization of clinics, improved utilization of resources, and clinic capacity. Adopting a personalized approach with reduced treatment burden may also lead to improvements in patient compliance.

The fundamental principles of an anti-VEGF treatment regimen were developed without consideration of resource limitations or practical barriers, i.e. if treating in an 'ideal' environment. Therefore, for practical application of the principles, it is important to identify and consider the barriers that might prove challenging for real-life implementation.

A treat-and-extend approach embodies the four fundamental principles of a treatment regimen, and is supported by the Vision Academy as the treatment of choice in retinal disease. However, for widespread adoption of this approach, payors and other stakeholders require more evidence of the benefits of the regimen in clinical practice. Reimbursement is a significant obstacle for many countries in the Asia-Pacific and Latin America regions, and also within Europe. Other barriers to the adoption of treat-and-extend include lack of consensus on criteria for disease stability and stopping treatment, and uncertainty regarding appropriate monitoring procedures.

The best evidence for treat-and-extend comes from treatment of neovascular AMD. Further clinical evidence is required to determine whether this treatment approach, or alternative treatment approaches that embody most of the principles, will offer the best outcomes for patients with RVO or DME and remain practical for the physician.



