

## 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](http://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.



Full consensus



Variations in opinion

## 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 patients<sup>1-7</sup>**
  - 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<sup>5,8-10</sup>**
  - 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' needs<sup>10-15</sup>**
  - 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

Vision Academy Viewpoints are intended to raise awareness of an unmet need within ophthalmology and provide an expert opinion to engage in further discussion.

They can be downloaded from <https://www.visionacademy.org/recommendations-and-resources>

The Vision Academy is sponsored by Bayer. This document reflects the views of a majority of Vision Academy members; individual views may vary.

The Vision Academy Steering Committee comprises Bora Eldem, Alex Hunyor, Antonia M. Joussea, Adrian Koh, Jean-François Korobelnik, Paolo Lanzetta, Anat Loewenstein, Monica Lövestam-Adrian, Rafael Navarro, Márcio Nehemy, Annabelle A. Okada, Ian Pearce, Francisco J. Rodríguez, Sebastian Wolf and David Wong.

Always refer to local treatment guidelines and relevant prescribing information.

The views represented in this document do not necessarily reflect those of Bayer.

January 2017 | G.COM.SM.STH.01.2017.1194

## References

1. Brown DM, Heier, *et al.* Intravitreal aflibercept 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.
2. Korobelnik J-F, Holz FG, Roeder 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.
3. 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.
6. 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): 1193–1203.
7. Lim JH, Wickremasinghe SS, Xie J, *et al.* Delay to treatment and visual outcomes in patients treated with anti-vascular endothelial growth factor for age-related macular degeneration. *Am J Ophthalmol* 2012; 153 (4): 678–686.
8. Hatz K and Prunte 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.
9. 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 age-related 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-and-extend protocol: Two-year results. *Ophthalmology* 2016; 123 (1): 51–59.
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): 1017–1028.
17. Engelbert M, Zweifel SA and Freund KB. "Treat and extend" dosing of intravitreal anti-vascular endothelial growth factor therapy for type 3 neovascularization/retinal angiomatous proliferation. *Retina* 2009; 29 (10): 1424–1431.



Full consensus



Variations in opinion

## 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**.<sup>16,17</sup>



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.

Vision Academy Viewpoints are intended to raise awareness of an unmet need within ophthalmology and provide an expert opinion to engage in further discussion.

They can be downloaded from <https://www.visionacademy.org/recommendations-and-resources>

The Vision Academy is sponsored by Bayer. This document reflects the views of a majority of Vision Academy members; individual views may vary.

The Vision Academy Steering Committee comprises Bora Eldem, Alex Hunyor, Antonia M. Jousens, Adrian Koh, Jean-François Korobelnik, Paolo Lanzetta, Anat Loewenstein, Monica Lövestam-Adrian, Rafael Navarro, Márcio Nehemy, Annabelle A. Okada, Ian Pearce, Francisco J. Rodríguez, Sebastian Wolf and David Wong.

Always refer to local treatment guidelines and relevant prescribing information.

The views represented in this document do not necessarily reflect those of Bayer.

January 2017 | G.COM.SM.STH.01.2017.1194