



Discussion: **Bilateral anti-VEGF treatment**

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Session aims

- To provide a summary of the Vision Academy's Viewpoint on bilateral anti-VEGF treatment
- To highlight the key barriers to implementing bilateral anti-VEGF treatment in clinical practice in Europe



An introduction to bilateral anti-VEGF treatment

- Many patients present with bilateral disease that is treatable with anti-VEGF agents
 - 1 in 4 unilateral AMD cases progress to bilateral disease within 5 years¹
 - Up to 1 in 2 unilateral late AMD cases progress to bilateral disease within 5 years¹
- Patients with bilateral neovascular AMD have reported substantially worse QoL²
- Treating each eye at separate visits adds significantly to the patient and clinic burden³
- Bilateral same-day injections are an appropriate and more convenient treatment option⁴

The Vision Academy defines bilateral anti-VEGF treatment as:

*“Simultaneous or consecutive administration of anti-VEGF treatment,
with both injections administered during the same patient visit”*



What is the Vision Academy's position?



Vision Academy Viewpoint: Bilateral anti-VEGF treatment

“Simultaneous or consecutive administration of anti-VEGF treatment, with both injections administered during the same patient visit”



It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions



The second injection should be treated as a separate procedure within the same visit



Compounded products should not be from the same batch



Extra care is required for patients who require bilateral injections at the first visit

Vision Academy Viewpoint: Practical guidance points

It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions



- There is **no evidence** to date to suggest that there is an increased risk of ocular events with bilateral compared with unilateral treatment^{1–5}
- There is **no evidence** that treating both eyes concomitantly alters the risk of systemic adverse events^{1,4,5}

The document is a white paper with a blue header. At the top left is the Vision Academy logo, which includes a stylized eye icon. To the right of the logo is the text 'VISION ACADEMY' and 'Society of Research & Education'. On the far right is the Bayer logo. Below the header, the title 'Bilateral Anti-VEGF Treatment' is centered. The main body of the document is divided into two columns: 'Background' and 'Viewpoint'. The 'Background' section discusses the commonality of bilateral anti-VEGF treatments and the lack of evidence for increased risks. The 'Viewpoint' section provides practical guidance, including:

- 1. It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions.
- 2. The second injection should be treated as a separate procedure within the same visit.

Both sections include footnotes and a small disclaimer at the bottom. The entire document is stamped with a large diagonal watermark reading 'Vision Academy'.



General consensus



Variation in opinion

1. Davis RP et al. *Clin Ophthalmol* 2010; 4: 703–707. 2. Abu-Yaghil NE et al. *Int J Ophthalmol* 2014; 7 (6): 1017–1021. 3. Lima LH et al. *Retina* 2009; 29 (9): 1213–1217.
4. Bayer plc. EYLEA 40 mg/mL solution for injection in a vial – summary of product characteristics; August 2016. 5. Ruão M et al. *Clin Ophthalmol* 2017; 11: 299–302.



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Vision Academy Viewpoint: Practical guidance points

The second injection should be treated as a separate procedure within the same visit



- Surgical disinfection of the surgeon's hands and/or application of new sterile gloves
- Application of povidone-iodine* to the conjunctival sac
- Cleaning of the periocular skin, eyelid margins and eyelashes with povidone-iodine*
- Use of sterile equipment, including masks, eyelid speculum, forceps, and ophthalmic drape¹

Background
Intravitreal injection is the most commonly performed ophthalmic procedure,¹ and injection of anti-VEGF agents is the gold standard treatment for many retinal vascular disorders. Clinical trials and real-life experience have demonstrated that single intravitreal injection can be very low risk of serious complications when proper procedures and precautions are followed.¹⁻⁴ However, many patients present with bilateral disease, raising the question of whether both eyes should be injected during the same visit.

Viewpoint

1. It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions

Bilateral treatment can be offered as simultaneous or consecutive administration of anti-VEGF treatment with both injections administered during the same patient visit. While some feel that this may pose an enhanced risk of local injection-related complications, there is no evidence to date suggesting that there is an increased risk of ocular adverse events with bilateral versus unilateral treatment.⁵⁻⁷ Furthermore, while there may be a theoretical risk of systemic adverse events associated with intravitreal injection of anti-VEGF agents, there is also no evidence that treating both eyes concomitantly alters this risk.⁸⁻¹¹ To manage the risks associated with the injection procedure, it is recommended to follow the guidance outlined in points 2-4 below in cases where bilateral treatment is deemed to be appropriate:

2. The second injection should be treated as a separate procedure within the same visit

To minimize the risk of procedure-related complications or cross-contamination between treatments, each injection should be treated as a completely new procedure. After the first injection, the patient should be repositioned and the recommended procedure for intravitreal injection. In brief, this should include:

- Surgical disinfection of the surgeon's hands and/or application of new sterile gloves
- Application of povidone-iodine¹ to the conjunctival sac
- Cleaning of the periocular skin, eyelid margins and eyelashes with povidone-iodine¹
- The use of sterile equipment, including mask, eyelid speculum, forceps, and ophthalmic drape (if used)¹⁻¹¹

*Or suitable alternative, such as chlorhexidine.

1. McCannel CA et al. Updated guidelines for intravitreal injection. Available at: http://www.reviewofophthalmology.com/content/d/retinal_insider/c/55627/. Accessed March 2017.



General consensus



Variation in opinion



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*Or a suitable alternative, such as chlorhexidine.

1. McCannel CA et al. Updated guidelines for intravitreal injection. Available at: http://www.reviewofophthalmology.com/content/d/retinal_insider/c/55627/. Accessed March 2017.

Vision Academy Viewpoint: Practical guidance points

Compounded products should not be from the same batch



- This is essential to avoid the risks of a contaminated product being administered to both eyes¹

Background
Intravitreal injection is the most commonly performed ophthalmic procedure,¹ and injection of anti-VEGF agents is the gold standard treatment for many retinal vascular disorders. Clinical trials and real-life experience have demonstrated that single intravitreal injection carry a very low risk of serious complications when proper procedures and precautions are followed.¹⁻⁴ However, many patients present with bilateral disease, raising the question of how to administer treatment.

Treating each eye at separate, staggered visits adds significantly to the burden of anti-VEGF therapy, essentially doubling both clinic time and cost.⁵ There is potential to substantially reduce this burden by treating both eyes during the same visit to the same patient visit. Furthermore, several studies have highlighted that patients prefer receiving treatment in this manner.⁵⁻⁷ Although the potential benefits are clear, the risks of bilateral anti-VEGF treatment have yet been fully characterized and evaluated. This viewpoint offers pragmatic clinical considerations that should help to mitigate any additional risk.

Viewpoint

- 1. It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions**
Bilateral treatment can be delivered as simultaneous or consecutive administration of anti-VEGF treatment with both injections administered during the same patient visit. While some feel that this may pose an enhanced risk of local injection-related complications, there is no evidence to date suggesting that there is an increased risk of ocular adverse events with bilateral anti-VEGF treatment compared to sequential treatment.⁵⁻⁷ Furthermore, while there may be a theoretical risk of systemic adverse events associated with intravitreal injection of anti-VEGF agents, there is also no evidence that treating both eyes concomitantly alters this risk.⁸⁻¹¹ To manage the risks associated with the injection procedure, it is recommended to follow the guidance outlined in points 2-4 below in cases where bilateral treatment is deemed to be appropriate.
- 2. The second injection should be treated as a separate procedure within the same visit**
To minimize the risk of procedure-related complications or cross-contamination between treatments, each injection should be treated as a completely new procedure. After the first injection, the patient should be cleaned again and the recommended procedure for intravitreal injection. In brief, this should include:
 - Surgical disinfection of the surgeon's hands and/or application of new sterile gloves
 - Application of povidone-iodine to the conjunctival sac
 - Cleaning of the periocular skin, eyelid margins and eyelashes with povidone-iodine¹²
 - The use of sterile equipment, including mask, eyelid speculum, forceps, and ophthalmic drapes (if used)¹²⁻¹⁴

*For instance antibiotics, such as ciprofloxacin.

1. McCannel CA et al. Updated guidelines for intravitreal injection. Available at: http://www.reviewofophthalmology.com/content/d/retinal_insider/c/55627/. Accessed March 2017.

2. The Vision Academy is a partnership between Bayer and Optivisio, specifically established with the aim of advancing key clinical needs in the field of retinal diseases. www.visionacademy.eu



General consensus



Variation in opinion



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1. McCannel CA et al. Updated guidelines for intravitreal injection. Available at: http://www.reviewofophthalmology.com/content/d/retinal_insider/c/55627/. Accessed March 2017.

Vision Academy Viewpoint: Practical guidance points

Extra care is required for patients who require bilateral injections at the first visit



- The preference of the patient should always be taken into account
 - There is a small risk that an idiosyncratic hypersensitivity response may occur after the first treatment
 - If possible, avoid bilateral injections until the tolerability of the agent has been ascertained
 - If bilateral treatment is essential at the first visit, consider separating the injections to allow time for acute hypersensitivity responses to manifest



General consensus



► Variation in opinion



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Vision Academy Viewpoint: Further considerations

Partial or lack of reimbursement

- Several countries reimburse only partially, or not at all, for bilateral injection procedures
- Physicians have no choice but to treat at separate visits, increasing the burden on patients, clinics, and healthcare systems
- The body of clinical data supporting safety and efficacy of bilateral anti-VEGF therapy must be further developed to enable payors to make informed choices about whether or not to reimburse treatment



General consensus



Variation in opinion

Vision Academy Viewpoint: Further considerations

Patients following different treatment regimens



- There is variation in opinion on how to address the needs of patients with bilateral disease who are following a treat-and-extend or PRN regimen
 - When extending treatment intervals, the needs of each eye should be considered separately
 - It may be preferable to treat both eyes according to the needs of the eye that requires the shortest interval

Code: VA_005

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VISION ACADEMY VIEWPOINT

The Vision Academy is a partnership between Sager and Optivision companies established with the aim of advancing key current events in the field of ocular disease. www.sagerassociates.com

Bilateral Anti-VEGF Treatment

Background

Intravitreal injection is the most commonly performed ophthalmic procedure,¹ and injection of anti-MFG agents is the gold standard treatment for macular edema associated with diabetic retinopathy, diabetic macula edema, and macular edema associated with central retinal vein occlusion.² Clinical trials and meta-analyses have demonstrated that single intravitreal injections carry a very low risk of systemic complications when proper procedures and precautions are followed.³⁻⁴ However, many patients present with bilateral disease, raising the question of whether treatment that both eyes require treatment.

Treatment of one eye at a time is a staggered series of visits due to the burden of anti-MFG therapy, essentially doubling both time and cost.⁵ Thus, it is potential cost to substantially reduce the burden by treating both eyes concomitantly at the same patient visit. Furthermore, several studies have shown that patients prefer having treatment in one visit.⁶⁻⁷ Although the potential benefits are clear, the risks of bilateral anti-VEGF treatment have not yet been thoroughly discussed and evaluated. This Viewpoint offers pragmatic clinical considerations that should help to mitigate any additional risk.

Viewpoint

1. It is possible and reasonable to conduct bilateral injections while observing appropriate procedures and precautions

Bilateral treatment can be defined as simultaneous or consecutive treatment of both eyes during a single visit. Both eyes can be injected simultaneously during a single visit. While it is true that this may pose an enhanced risk of local injection-related complications, there is no evidence to date suggesting that there is an increased risk of ocular adverse events with bilateral treatment compared with unilateral treatment.^{8,9,10} Furthermore, while there may be a theoretical risk of systemic adverse events associated with intravitreal regimens, this risk is minimal, as the drug is rapidly cleared from both eyes concomitantly after the visit.¹⁰⁻¹² To manage the risks associated with the injection procedure, it is recommended to follow the guidance outlined in points 2-4 below in cases where bilateral treatment is deemed to be appropriate.

2. The second injection should be treated as a separate procedure within the same visit

To minimize the risk of procedure-related complications or cross-contamination between treatments, each injection should be treated as a completely new procedure. After the first injection, the patient should be prepared again, following the recommended procedure for intravitreal injections. In brief, this should include:

- Surgical dissection of the surgeon's hands and/or application of new sterile gloves
- Application of povidone-iodine¹³ to the conjunctival sac
- Cleaning of the periocular skin, eyelid margins and eyelashes with povidone-iodine¹⁴
- The use of sterile equipment, including masks, eyelid speculum, torque, and ophthalmic drape (if used)¹⁴⁻¹⁶

3. Employment of a surgical alternative, such as ophthalmic

Employed by the Vision Academy
in January 2016.
Date of review: January 2018

4. Bilateral treatment is safe and effective

*Or surgical alternative, such as ophthalmic

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The Vision Academy Review Committee comprises Ira Sager, Alan Hargan, Anthony W. Johnson, Andrew J. Myerson, Narendran Kandasamy, Paul Lefebvre, and Lawrence M. Rosenbaum. The Vision Academy is a partnership between Sager and Optivision companies. Ira Sager, Alan Hargan, Anthony W. Johnson, Andrew J. Myerson, Narendran Kandasamy, Paul Lefebvre, and Lawrence M. Rosenbaum are members of the Vision Academy Review Committee and receive fees.

Designers of the visual treatment guidelines and research protocols themselves.

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products should not be from the same batch
If the risk of a contaminated product being released is especially important, we recommend to acquire them into individual doses or products personalized to each eye should be used.

supplied in packages for single use
In very large lot sizes, no use of containers is advised that this is the case, separate packages that require bilateral

use to reduce injections in both eyes of the patient should always be given to treat both eyes at once if that is an idiopathic side effect
If until the invariability of the use treatment at the first visit for acute or exacerbating the last or separated at the end

failure of the treatment
can be obtained to treat both eyes simultaneously under supervision of all. By no duration can treatment be interrupted body of

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SAFER



General consensus



• Variation in opinion

Summary



The **Vision Academy Viewpoint** offers practical guidance that should help to mitigate any additional risks associated with bilateral anti-VEGF injections



The body of clinical data supporting safety and efficacy of bilateral anti-VEGF therapy must be further developed to enable payors to make informed choices about whether or not to reimburse treatment



There is variation in opinion on how to address the needs of patients with bilateral disease who are following a **treat-and-extend** or **PRN** regimen



General consensus



Variation in opinion



Discussion

