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

Evolving Clinical Practice: Insights Gained from Real-World Evidence

Background

New pharmacological treatments are typically approved following evaluation in randomized controlled trials (RCTs), which aim to investigate the efficacy and safety of treatments in specific well-controlled target populations over relatively short time periods.

Real-world data (RWD) are routinely collected data from sources other than RCTs and are related to patient health status and/or healthcare delivery.[1] RWD can be analyzed to produce real-world evidence (RWE), which provides information on the use and potential benefits and risks of a treatment under real-world conditions, often in diverse populations.[1,2]

RWE is particularly important in retinal disease as it can help in the continual assessment of real-world treatment regimens in order to improve patient outcomes and reduce treatment burden.

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Viewpoint

There is a need for real-world studies to complement the findings from RCTs by examining interventions under conditions that closely reflect the heterogeneous patient populations and the less-standardized treatment protocols associated with clinical practice.[3]

As well as generating effectiveness data, real-world studies can also generate information on other topics of interest, including variation in practice patterns, patient-related outcomes such as quality of life, cost–benefit ratio, and the influence of varied patient characteristics on outcomes.

RWE can often be better generalized to typical clinical practice than evidence from RCTs[4,5]

RCTs: Can the treatment work?	RWE: Does the treatment work?
• Selected patient population with strict inclusion and exclusion criteria • Protocol-driven treatment in an "ideal setting" designed to meet the requirements of regulators and payers • Treatment and placebo may not reflect clinical practice • Intervention is strictly enforced and standardized • Not well suited to assess treatment safety	• Diverse, unselected population with few to no exclusion criteria • Routine clinical practice, allowing for investigation of clinically relevant indications • Treatment(s) of interest may reflect options used in clinical practice, not the treatments in clinical trials • Intervention is at the discretion of the treating physician • Can provide the statistical power to assess treatment safety

In retinal disease, real-world studies evaluating the management of neovascular age-related macular degeneration (nAMD) have informed dosing strategies with anti-vascular endothelial growth factors (VEGFs) in clinical practice, highlighting that visual outcomes achieved with anti-VEGFs in clinical practice sometimes differ from those derived from RCTs.[6-8] Collectively, real-world studies of aflibercept and ranibizumab have:

- Highlighted that in clinical practice, treatment regimens differ from the regular fixed dosing used in RCTs, and irregularities in dosing and treatment strategies are associated with worse outcomes when compared with regular dosing[8,9]
- Helped to optimize visual outcomes and minimize injection frequency through the use of treat-and-extend (T&E) dosing of anti-VEGF agents[10-12]
- Provided useful information regarding the time to reactivation of nAMD when anti-VEGF treatment is discontinued[13,14]

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In the PERSEUS,[6] RAINBOW,[7] and LUMINOUS[8] studies, 69–76% of patients were not treated with regular treatment. Regular treatment in these studies was associated with greater improvements in visual acuity compared with irregular treatment regimens.[6-9] These data suggest that, in practice, treatment was largely administered following different and irregular protocols, and these irregularities are associated with worse outcomes compared with regular dosing, supporting the need for regular proactive treatment.

Studies looking at a T&E dosing regimen have also shown improvements in visual outcomes, while also reducing hospital visits and showing a trend for reductions in caregiver burden, time, and costs.[10-12] This RWE supports the use of T&E dosing of anti-VEGF agents as a way of optimizing visual outcomes while minimizing injection frequency.

An analysis of large data sets in the Fight Retinal Blindness! Registry confirmed a high rate of disease reactivation over time after disease stability was achieved and anti-VEGF treatment ceased.[13,14] These data provide useful information regarding the time to reactivation of nAMD when anti-VEGF treatment is discontinued.

These and similar insights have informed regulatory and clinical decision making for the management of retinal disease and emphasize the importance of both RCTs and RWE in improving patient outcomes and reducing the treatment burden of retinal disease.

Further considerations

RWD can be collected prospectively for a specific research purpose (known as primary RWD) or retrospectively from different sources that contain data collected for other purposes (known as secondary RWD).[3] The majority of RWD sources are electronic, and recent technological advances make systematic data collection increasingly easy and accessible. However, the increased availability of RWD needs to be balanced against the data integrity and usability, and the complexity and robustness of data sources need to be considered when using RWD.

Understanding the strengths and limitations of each data source is critical for researchers using RWD to supplement data from RCTs.

Vision Academy Viewpoints are intended to raise awareness of a clinical challenge within ophthalmology and provide an expert opinion to engage in further discussion.
They can be downloaded from https://www.visionacademy.org/resource-zone/resources/all
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Always refer to local treatment guidelines and relevant prescribing information.
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