Understanding Real-World Evidence for Safety, Efficacy, and Adherence of Anti-Vascular Endothelial Growth Factor in Wet Age-Related Macular Degeneration: A Scoping Review

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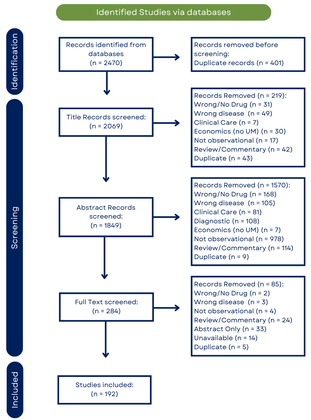
Background

- Anti-Vascular Endothelial Growth Factor (VEGF) therapies inhibit VEGF in angiogenesis.[1] This pathway blocks microvasculature regulation and maintenance signaling, leading to adverse effects.[2]
- The economic value of these medications in wet age-related macular degeneration (AMD) suggests increased utilization could improve patients' economic and clinical burden.[3]
- Studies demonstrate safety, efficacy, and benefits. However, their short half-life, frequent dosing, and potential side effects pose challenges, and the real-world impact is unclear.

Objective

To observe treatment patterns, clinical outcomes, and safety profiles across diverse patient populations. Secondarily, to understand dosing frequency and adherence patterns.

Methods



- Scoping review conducted according to the PRISMA-ScR framework.
- All peer-reviewed articles published in English through March 9, 2025, were included.
- Records (n = 2,470) were identified in PubMed, EMBASE, Cochrane Library, CINAHL, and Web of Science with the keywords: bevacizumab, ranibizumab, aflibercept, brolucizumab, faricimab, Wet Age-Related Macular Degeneration, administrative claims, real-world, and observational.
- Overall trends in utilization pattern, clinical outcomes, and research landscape are summarized.

Results

Research Landscape	
Characteristics	n (%)
Drug	
Bevacizumab	68 (35.4%)
Ranibizumab	122 (63.5%)
Aflibercept	110 (57.3%)
Faricimab	12 (6.3%)
Brolucizumab	12 (6.3%)
Unspecified	22 (11.15%)
Location	
Europe	129 (67.2%)
North America	52 (27.1%)
Asia	34 (17.7%)
Middle East	8 (4.2%)
Oceania	45 (23.4%)
Data Source	
Electronic Medical Record	61 (31.8%)
Registry	52 (27.1%)
Claims Data	25 (13.0%)
Database	62 (32.3%)

Utilization Patterns

Patient Population [Majority]	**Age**	**Gender**	**Race**	**Lost to Follow-Up**
	≥ 75 years	Female	White	Black; Medicaid; Low-Income/Rural
Treatment Regimen	**# Injections in Year 1**	**Injection Interval**	**Agent Used Most Often**	**Efficacy of Loading Dose**
	7 injections (mean)	4-12 weeks	Ranibizumab > Aflibercept > Bevacizumab	Cannot be Determined

Clinical Outcomes

Efficacy – Primary Outcomes

Visual Acuity	• No significant difference between agents • Range of Early Treatment Diabetic Retinopathy Study-equivalent (ETDRS) letters gained: +1-9 letters	**Central Retinal Thickness**	• Range of reduction over 12 months: 2-49 µm • Significant reduction after 1 year of treatment
Intra-Ocular Pressure	• Decrease: aflibercept • Increase: ranibizumab • Variable effect: bevacizumab	**CNV Inactivity**	• Agents studied: ranibizumab and aflibercept – similar effect • Lesion inactivity over 2-3 years: ~50% • Median time to lesion inactivity: 15 weeks (ranibizumab), 71 days (aflibercept)

Safety – Adverse Events

<1%	• Endophthalmitis • Uveitis & vitreous hemorrhage • Submacular hemorrhage	**≥1%**	• Myocardial Infarction/Stroke/All-Cause Mortality: bevacizumab > ranibizumab ≥ aflibercept • Kidney failure/disease: bevacizumab > aflibercept > ranibizumab

Conclusion

- Anti-VEGF therapies are safe and effective for wet-AMD.
- Utilization, safety, and efficacy among aflibercept, bevacizumab, and ranibizumab have remained steady over time.
- Ranibizumab had the highest number of injections and bevacizumab had the lowest.
- There are overall improvements in VA/BCVA, but evidence there is still loss of ETDRS letters with treatment.
- Brolucizumab and faricimab are new anti-VEGF therapies that need more studies to determine their safety and efficacy against aflibercept, bevacizumab, and ranibizumab.

References

A complete list of studies that were included in the final analysis may be found via this QR code:

1. Campa C, P. Harding S. Anti-VEGF Compounds in the Treatment of Neovascular Age Related Macular Degeneration. Curr Drug Targets. 2011;12(2):173-181.
2. Kamba T, McDonald DM. Mechanisms of adverse effects of anti-VEGF therapy for cancer. Br J Cancer. 2007;96(12):1788-1795.
3. Mulligan K, Seabury SA, Dugel PU, Blim JF, Goldman DP, Humayun MS. Economic Value of Anti–Vascular Endothelial Growth Factor Treatment for Patients With Wet Age-Related Macular Degeneration in the United States. JAMA Ophthalmol. 2020;138(1):40–47. doi:10.1001/jamaophthalmol.2019.4557

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