

SUPPLEMENTARY MATERIAL

Systemic Effects of Intravitreal Anti-VEGF Therapy: A Review of Safety Across Organ Systems

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Appendix

A systematic literature search was conducted using the **MEDLINE** database accessed via **PubMed**. The search focused on the pharmacokinetics, pharmacodynamics, and systemic side effects of intravitreal anti-VEGF therapy, particularly concerning renal, cardiovascular, and neuronal health.

Search Terms and Boolean Operators

The following search terms and Boolean operators were used:

1. Pharmacokinetics & Pharmacodynamics

- ("Anti-VEGF" OR "vascular endothelial growth factor inhibitor" OR "bevacizumab" OR "ranibizumab" OR "aflibercept" OR "faricimab" OR "brolucizumab")
- AND ("pharmacokinetics" OR "systemic absorption" OR "half-life")
- AND ("pharmacodynamics" OR "biological effects")

2. Systemic Safety Concerns

- ("Anti-VEGF" OR "intravitreal anti-VEGF")
- AND ("renal effects" OR "kidney function" OR "glomerular filtration rate")
- OR ("cardiovascular effects" OR "myocardial infarction" OR "stroke" OR "thromboembolic events")
- OR ("central nervous system effects" OR "neurological complications" OR "blood-brain barrier")

3. Safety in Special Populations

- ("anti-VEGF" OR "intravitreal anti-VEGF")
- AND ("pregnancy" OR "breastfeeding" OR "lactation" OR "fetal development")
- OR ("retinopathy of prematurity" OR "ROP" OR "neonatal safety")

4. Inclusion Criteria

- Articles published in English up to **January 2025**

- Studies analyzing pharmacokinetics, pharmacodynamics, and systemic safety of anti-VEGF therapy
- Research on renal, cardiovascular, and neurological effects
- Studies discussing safety in pregnancy, breastfeeding, and ROP

5.Exclusion Criteria

- Non-English articles
- Conference abstracts, commentaries, and editorial letters
- Animal studies unless relevant to systemic safety concerns

6.Study Selection Process

- Titles and abstracts of identified studies were **independently screened** by two authors (**MB and SKP**) to assess relevance.
- Full-text reviews were conducted for eligible articles.
- Duplicates and irrelevant studies were removed.
- The selection process adhered to the **ENTREQ checklist for qualitative studies**, ensuring a rigorous and systematic approach.