A Tale of Two Eyes: Macular Atrophy Following Frequent Anti-VEGF in Neovascular AMD

Author: **Nicolas Nicolaou**
Cambridge University Hospitals

The ROYAL COLLEGE of OPHTHALMOLOGISTS

Annual Congress 2026 18–21 May Manchester Central

BACKGROUND

Macular atrophy (MA) causes irreversible visual loss in Age-related Macular Degeneration (AMD).

Risk Factors of MA

- Genetic predisposition
- Smoking,
- Hypercholesterolaemia
- Age >80 years
- Drusenoid subretinal deposits (bilateral)
- Pigment epithelial detachment (PED)
- Choroidal thinning
- **Frequent Anti-VEGF 3**

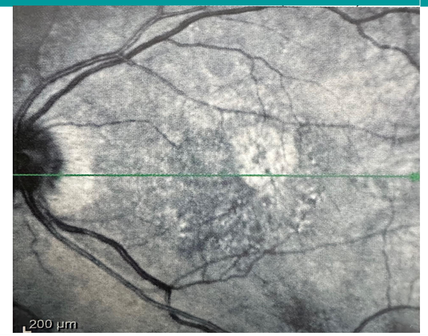
Monthly Anti-VEGF treatment for nAMD increases Macular Atrophy by 30%.

Anti-VEGFs are essential treatment for neovascular nAMD and should not be withheld.[1-3]

However, several large trials (CATT, IVAN,HABOR) indicate Anti-VEGF therapy is an **Additional risk factor for Macular Atrophy.** [1-4]

The incidence of MA increases by 29% with frequent monthly intravitreal injections (IVT).[1,3]

True incidence of MA with **short acting** versus **long-acting Anti-VEGFs** is underreported and may be subject to publication bias and cost.



OBJECTIVE & METHODS

Objective:

- To highlight the increased risk and rate of progression of MA associated with frequent use of short acting Anti-VEGF agents.
- To advocate for replacement with long-acting alternatives within national health services for these high-risk patients.

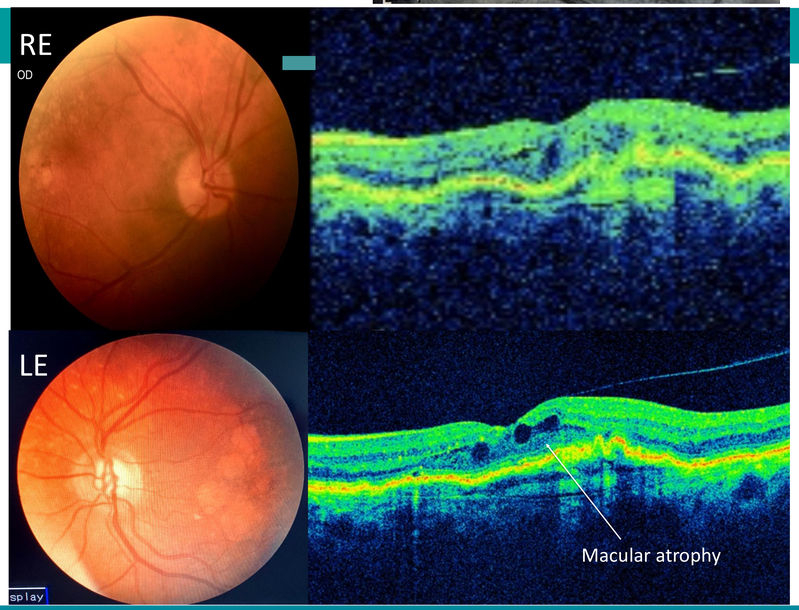
Methods: A literature search and retrospective cases of MA following frequent IVT injections was reviewed.

RESULTS

A high-risk patient: 81-year-old smoker with bilateral drusenoid subretinal deposits also developed neovascular AMD (nAMD) in the left eye.
Baseline BCVA was 6/9 (0.22 logMAR) OD and 6/12 (0.30 logMAR) OS.
Left eye received 19 bevacizumab IVT over 25 months. He developed MA, with vision declining to 3/60 (1.30 logMAR).
The right eye, with non-neovascular (dry) AMD, developed only mild atrophy and maintained stable vision at 6/12 (0.30 logMAR).

Literature search

Across 23 studies the pooled 24-month incidence of MA following Anti-VEGF therapy was 29% (95% CI: 20–38%)[2]
Monthly dosing was associated with a higher MA risk (29%) compared with extended regimens (14–17%)[2,3]
Subretinal fluid (SRF) >25 µm without intraretinal fluid was associated with a significantly lower risk of MA ($p < 0.001$), suggesting a protective effect.
Anti-VEGF reduce subretinal fluid implicating frequent Anti-VEGF injections increase risk of MA.[2-5]



Conclusion

- **Macular atrophy (MA)** currently has no approved pharmacological treatment.
- Evidence suggests that anti-VEGF therapy represents an additional risk factor, with up to 1 in 3 patients developing MA within two years.
- **Frequency rather than type of anti-VEGF agent appears to increase risk.**
- While short-acting anti-VEGF agents are cost-effective, frequent dosing is linked to greater choroidal thinning and less SRF leading to *less protective effect* and earlier progression of MA than longer-acting regimens.
- Health policy for treatment of nAMD **should prioritise long-acting Anti-VEGF agents** (Aflibercept, Faricimab) to reduce MA progression in high-risk patients, despite higher costs.

REFERENCES

1. Bro T, Derebecka M, Jørstad ØK, Grzybowski A. Off-label use of bevacizumab for wet age-related macular degeneration in Europe. *Graefes Arch Clin Exp Ophthalmol*. 2020;258:503–511.
2. Berni A, Coletto A, Li J, et al. Macular atrophy in neovascular age-related macular degeneration: a systematic review and meta-analysis. *Ophthalmol Retina*. 2025;9:625–644.
3. Foss A, Rotsos T, Empeslidis T, Chong V. Development of macular atrophy in patients with wet age-related macular degeneration receiving anti-VEGF treatment. *Ophthalmologica*. 2022;245:204–217
4. **Sadda SR, Abdelfattah NS, Lei J, *et al.*** Spectral-domain OCT risk factors for macular atrophy in HARBOR. *Ophthalmology*. 2020;127:1360–1370. doi:10.1016/j.ophtha.2020.03.031..
5. **Mehta NN, Nagel ID, Agnihotri A, *et al.*** Anti-VEGF injections and macular atrophy progression in neovascular AMD in remission. *Br J Ophthalmol*. 2025;109:1028–1035. doi:10.1136/bjo-2024-326124