

What variables affect the half-life of intravitreal medications?

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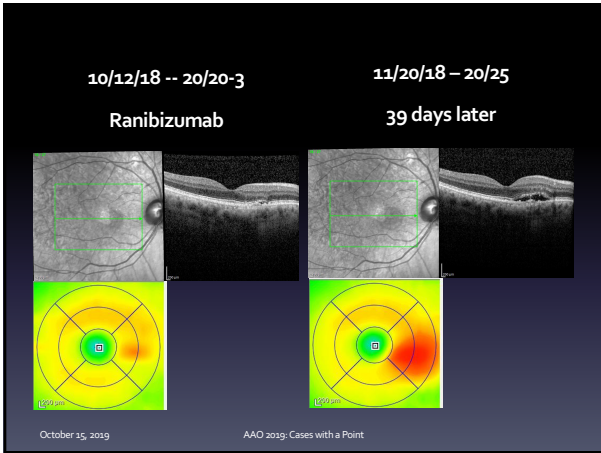
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70 y/o M

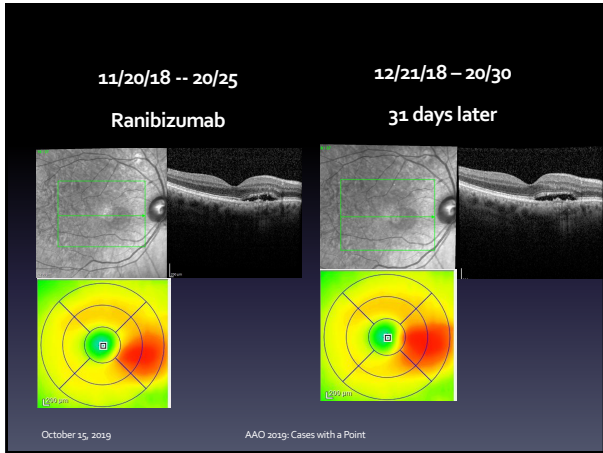
- 10/12/18: 5 weeks s/p Lucentis #6 OD
 - Increased fluid seen when his Rx interval was extended to 6 weeks.
 - Va 20/20-3 OD 20/20-2 OS
 - Combigan OU BID; Lumigan OU QHS; Restasis OU BID.
 - Lisinopril; Lipitor; HCTZ; Protonix

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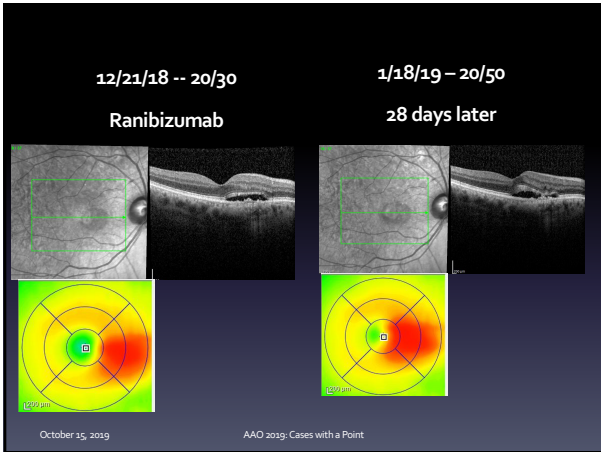
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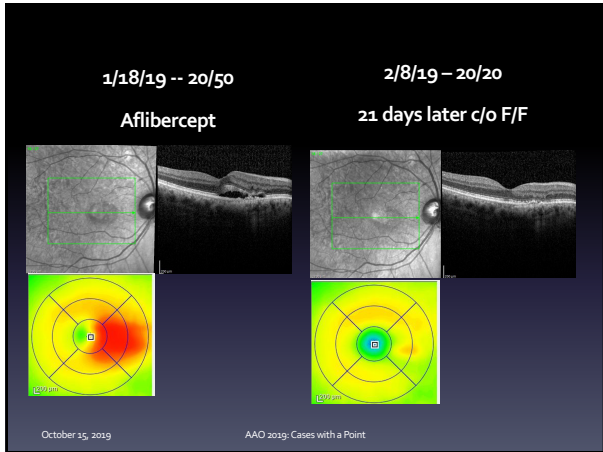
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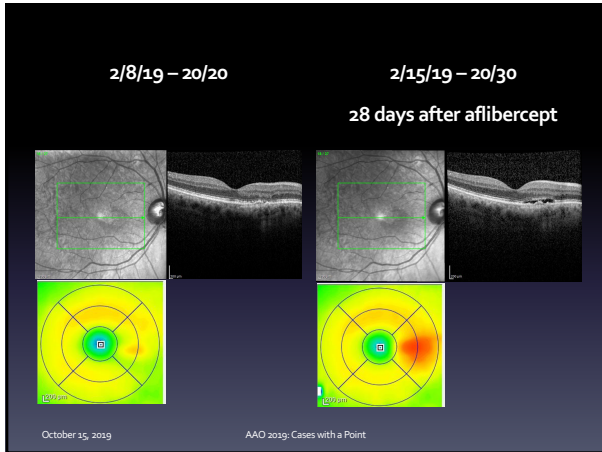
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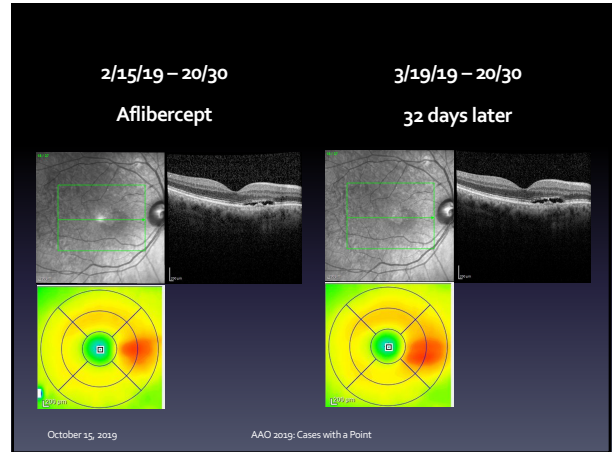
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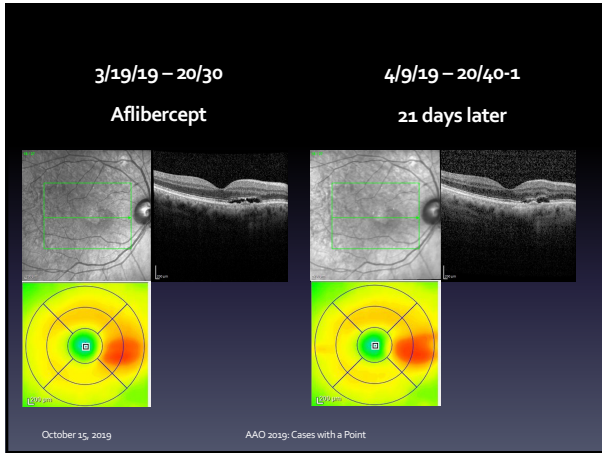
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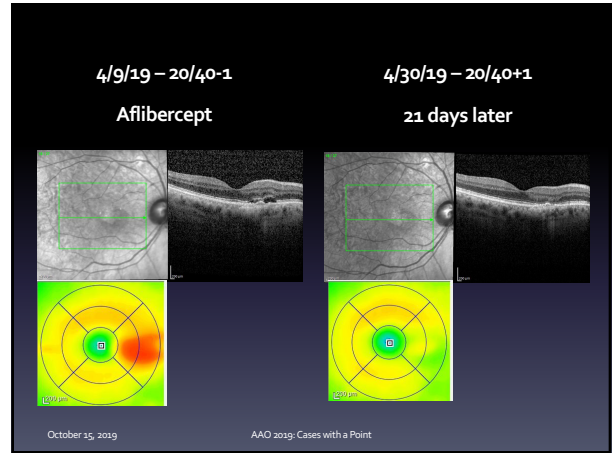
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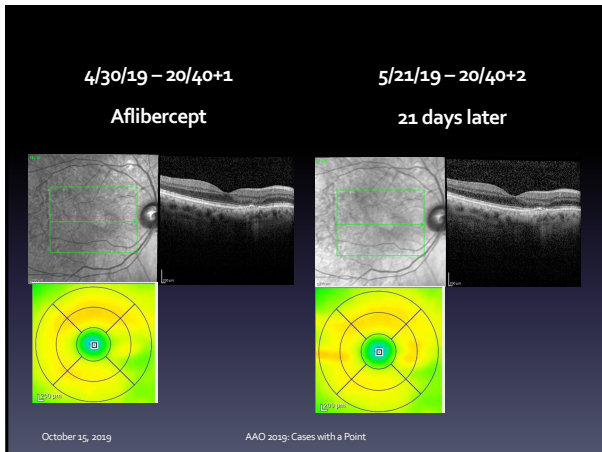
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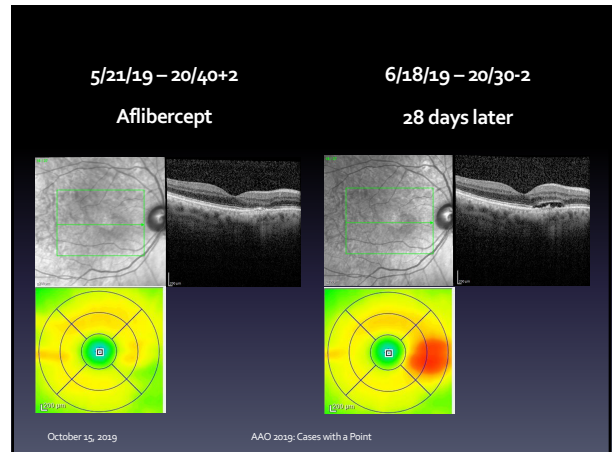
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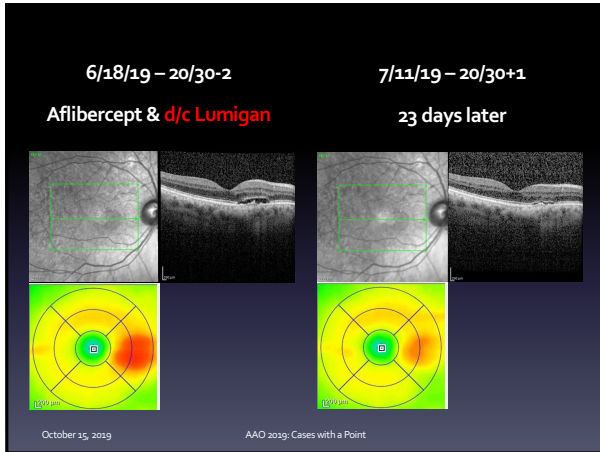
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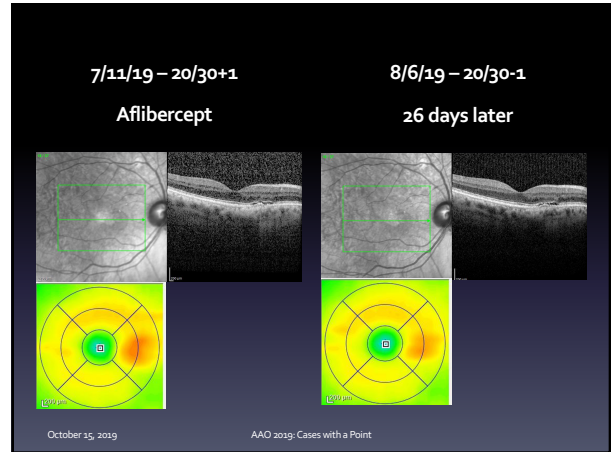
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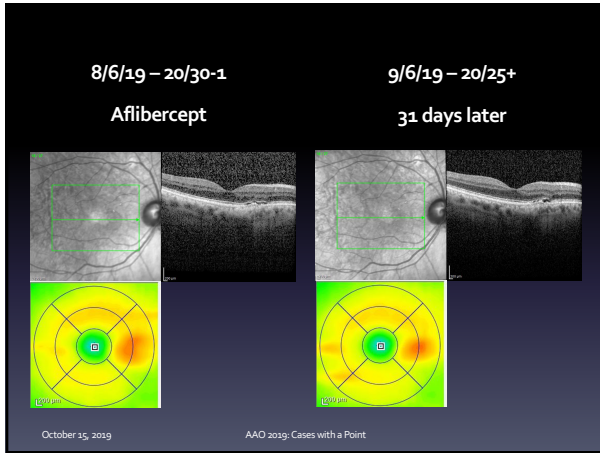
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Gaudreault J, Fei D, Beyer JC et al. Pharmacokinetics and retinal distribution of ranibizumab, a humanized antibody fragment directed against VEGF-A, following intravitreal administration in rabbits. *Retina* 2007;27:1260-1266.

- Autoradiographic findings showed rapid and persistent diffuse distribution of radiolabeled ranibizumab **through all retinal layers**, including the retinal pigment epithelial cell layer. Localization of radiolabeled ranibizumab was also observed in the ganglion cell layer, the inner and outer nuclear layers, and photoreceptor, with penetrations to the choroids. Other sites of distribution included the **optic nerve head** and **optic nerve**, **ciliary body** epithelium and stroma, and **corneal endothelium**.

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Impact of Concomitant Aqueous Suppressants on PRN Treatment With Ranibizumab in the 24 Month HARBOR Study

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Figure 1. Potential mechanism for the prolonging of ranibizumab's intraocular presence and clinical effect by aqueous suppressants.

Clearance from eye via choroid or aqueous humor outflow

Reduced clearance from eye via aqueous humor outflow, prolonging presence of ranibizumab in the eye

Table 1. Total numbers of patients using at any time vs. not using at any time concomitant beta-blockers or carbonic anhydrase inhibitors during the HARBOR study.

	Non-use, n	Use, n
Beta-blocker, oral*	299	176
Carbonic anhydrase inhibitor, oral	473	2
Beta-blocker, topical	453	22
Carbonic anhydrase inhibitor, topical	469	6
Cosopt†	474	1

*Including patients with any use of other aqueous suppressants: beta-blocker oral use, n=279 patients; non-use, n=175 patients.
†Cosopt is a topically-administered combined carbonic anhydrase inhibitor and beta-blocker, containing dexamethasone and timolol.

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Dorzolamide-Timolol vs Placebo Drops as an Adjunct to Intravitreal Anti-Vascular Endothelial Growth Factor Injections for Incomplete Responders with Neovascular Age-Related Macular Degeneration
Jason Hsu, Samir Patel, Turner Wibbelsman, Thomas Jenkins, Anthony Obeid, Jeremy D. Wolfe, Chirag P. Shah, Eric Chen on behalf of the DAWN Study Group

Methods: This prospective, multicenter randomized clinical trial enrolled patients with neovascular AMD and persistent macular edema despite frequent fixed-interval intravitreal anti-VEGF therapy. Eyes were randomized to use topical dorzolamide-timolol twice daily or artificial tears twice daily for the duration of the study. At each visit, anti-VEGF injections were continued with the same fixed interval and agent as before the

Conclusions: Topical dorzolamide-timolol appears to reduce macular edema in eyes with persistent exudation despite consistent, fixed-interval intravitreal anti-VEGF treatment for neovascular AMD.

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Figure 1. Potential mechanism for the prolonging of ranibizumab's intravitreal presence and clinical effect by aqueous suppressants.

- Brimonidine
 - ↓'s aqueous production & ↑'s uveoscleral outflow
- Timolol
 - ↓'s aqueous production
- CAI (Dorzolamide)
 - ↑'s RPE pump
 - ↓'s aqueous production
- Bimatoprost
 - ↑'s uveoscleral outflow

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In incomplete anti-VEGF responders → consider stopping prostaglandin analogs?

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