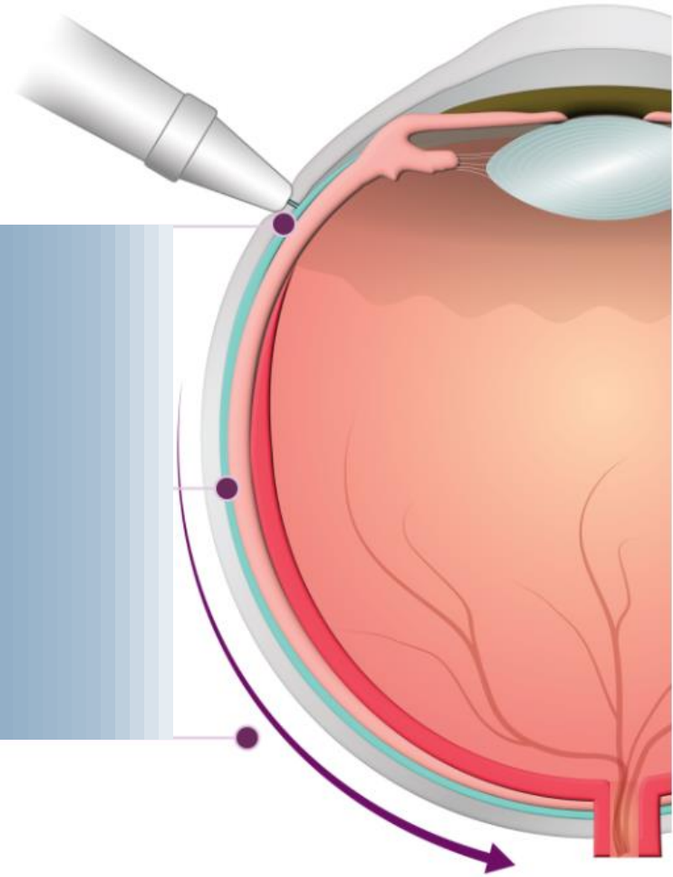
UCDAVIS EYE CENTER

Suprachoroidal drug delivery in the Real World



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Dept. of Ophthalmology
UC Davis Health
Sacramento, CA

Clinical Trials @ Summit
Park City, UT
June 8th, 2024

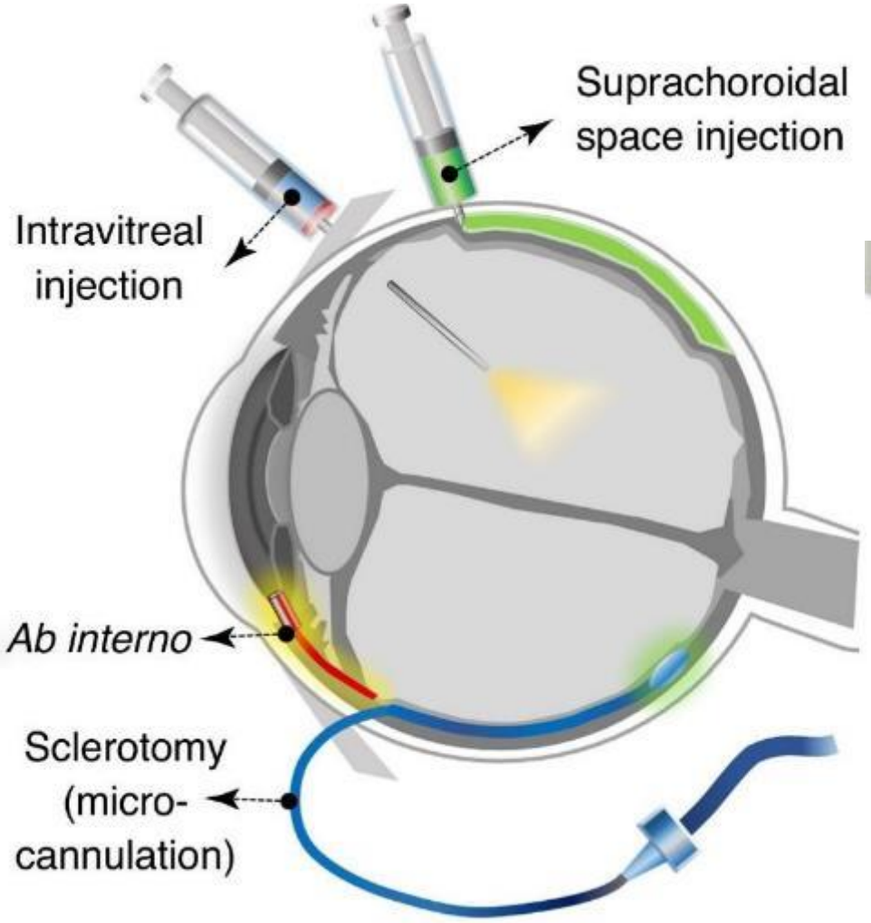
Financial Disclosures

- I have the following financial interests or relationships to disclose:
  - 4DMT: Consultant/Advisor
  - **Abbvie: Consultant/Advisor**
  - Adverum: Consultant/Advisor
  - Alimera Sciences, Inc.: Consultant/Advisor
  - **Bausch + Lomb: Consultant/Advisor**
  - Boehringer Ingelheim: Consultant/Advisor
  - **Clearside Biomedical, Inc.: Consultant/Advisor**
  - Endogena: Consultant/Advisor
  - GENENTECH: Consultant/Advisor
  - Gyroscope Therapeutics: Consultant/Advisor
  - IRIDEX: Consultant/Advisor
  - Janssen Pharmaceuticals, Inc.: Consultant/Advisor
  - jCyte: Consultant/Advisor
  - Myrobalan: Consultant/Advisor
  - NGM Biopharmaceutical: Consultant/Advisor
  - Novartis Pharma AG: Consultant/Advisor
  - Ocuphire: Consultant/Advisor
  - Ray Therapeutics: Consultant/Advisor
  - **RegenXBio: Consultant/Advisor**
  - Stealth Therapeutics: Consultant/Advisor
  - West: Consultant/Advisor

Accessing the suprachoroidal space

Microcatheter

orbitsds.com

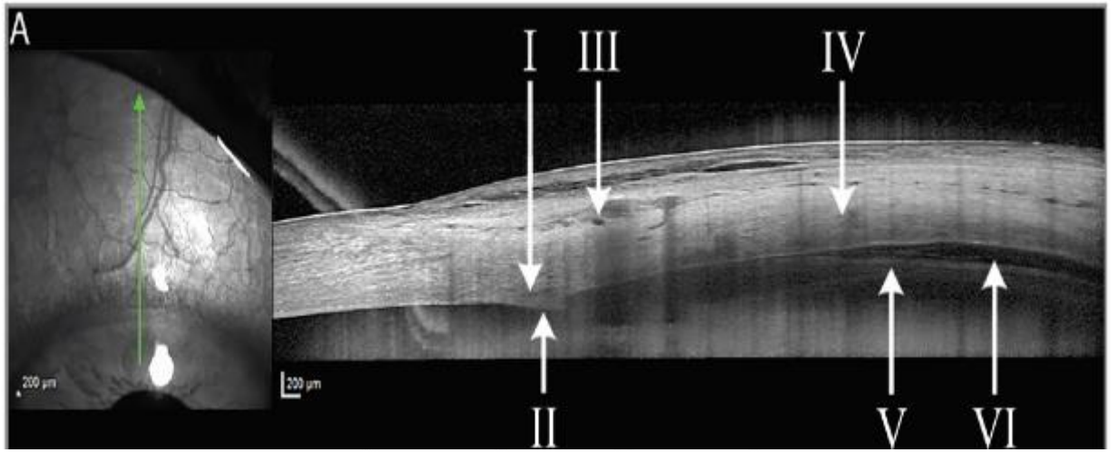


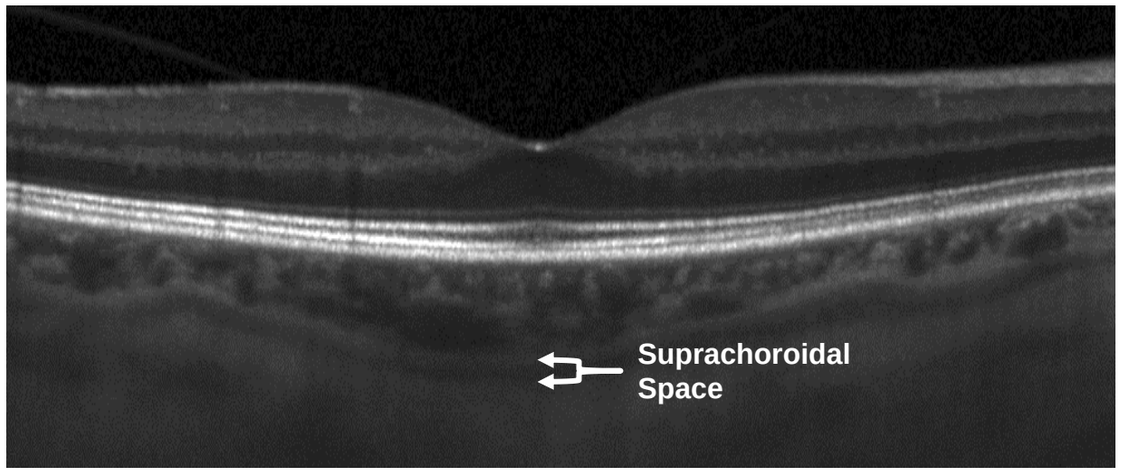
Microneedle

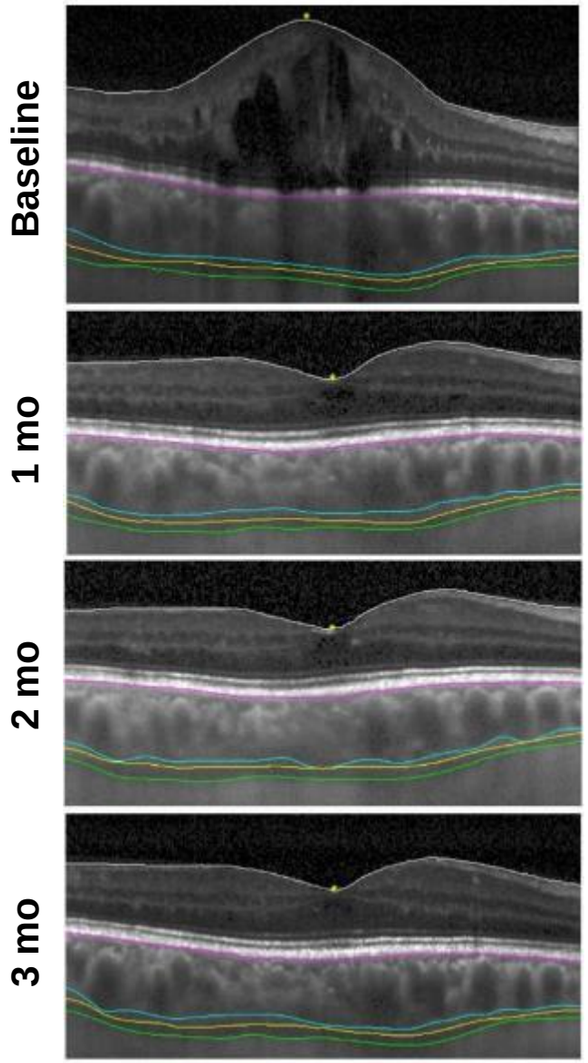
clearsidebio.com

Jung et al., *Drug Discovery Today*, 2019
Naftali & Moisseiev, *Pharmaceutics*, 2021

OCT shows SCS expansion after SC injection in humans



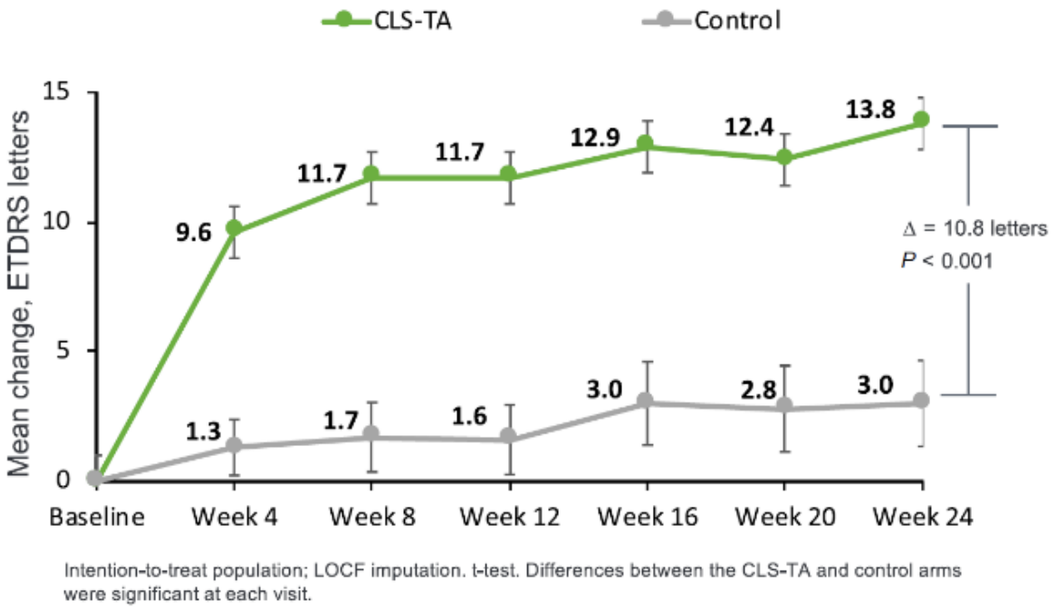




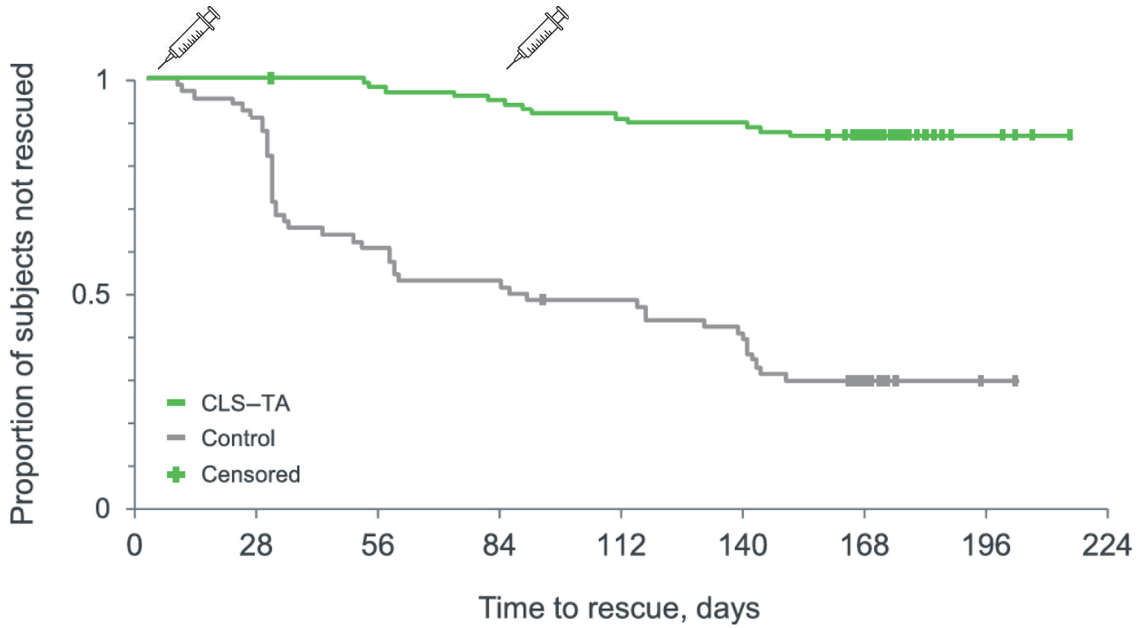
Lampen et al. *OSLI Retina*, 2018
Yiu et al., *Am J Ophthalmol*, 2018

Suprachoroidal Triamcinolone (CLS-TA) for Uveitic ME

Phase 2 TANZANITE study	Phase 3 PEACHTREE study	Phase 1/2 HULK study	Phase 1/2 OASIS study
RVO + CME	**Uveitic ME**	DME	nAMD



Intention-to-treat population; LOCF imputation. t-test. Differences between the CLS-TA and control arms were significant at each visit.



N = 160 patients with uveitic CME
Suprachoroidal CLS-TA vs. sham (3:2) at day 0 & week 12

Yeh et al., *Ophthalmol*, 2020

IRIS study of real-world durability of suprachoroidal triamcinolone for uveitic ME

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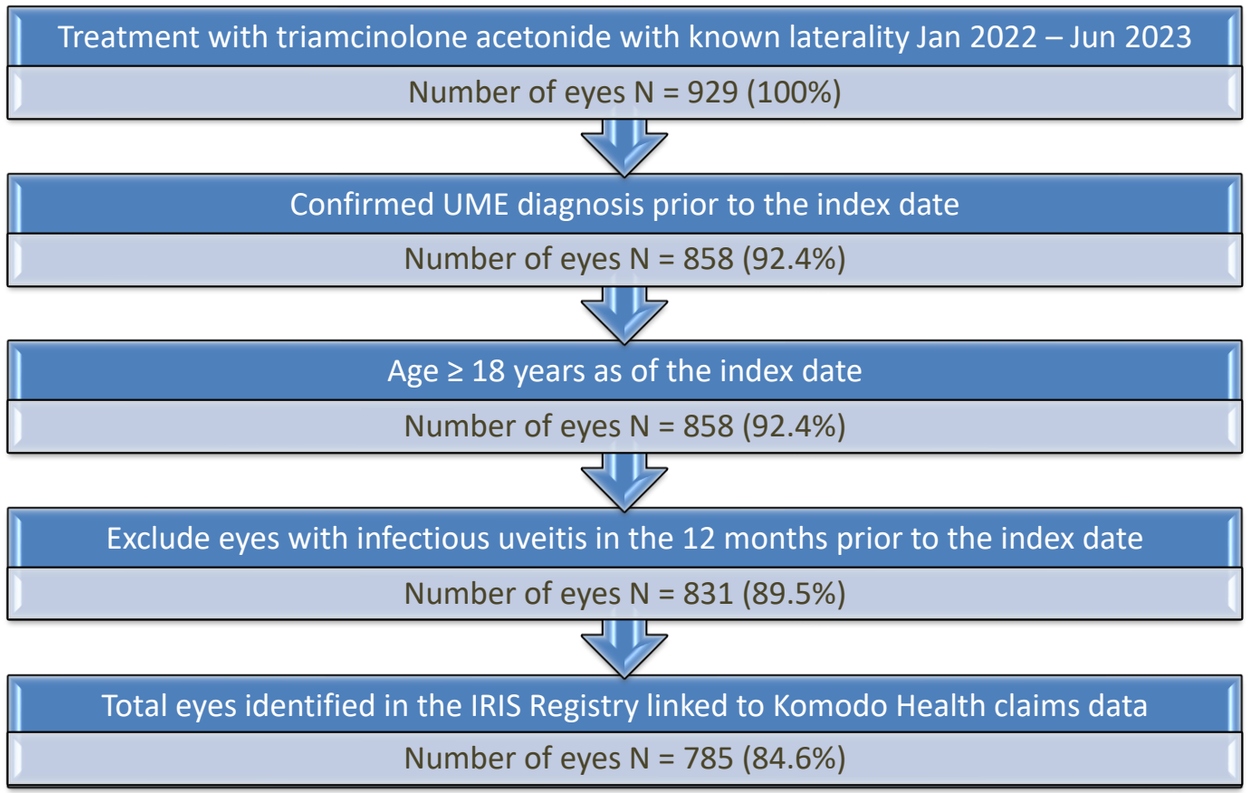
Inclusion criteria

- age ≥18 years
- diagnosis of non-infectious UME
- suprachoroidal triamcinolone inj

Study Design

- Dates: Jan 2022 to Jun 2023
- Index date: first suprachoroidal triamcinolone acetonide injection
- Rescue: any injectable, implanted, or topical cortical steroids
- Follow-up: 24 weeks

IRIS® Registry (Intelligent Research in Sight) linked to Komodo open-source claims data using the Datavant token to identify corticosteroid use



Study demographics & comorbidities

Total eyes	831 (100.0%)
Age	
Mean (SD)	68.2 (13.6)
Sex	
Female	55.7%
Male	44.3%
Race	
Asian	1.7%
Black or African American	9.4%
White	65.8%
Other races	8.3%
Unknown	14.8%
Ethnicity	
Hispanic	4.8%
Non-Hispanic	64.7%
Unknown	30.4%
Insurance / payer type	
Medicare	53.4%
Medicare Advantage	9.7%
Medicaid	4.6%
Commercial	26.0%
Other/Unknown	6.3%

Abbreviations: SD, standard deviation

Ocular comorbidities	
Glaucoma/Ocular Hypertension	41.8%
Cataract	24.7%
nAMD	2.3%
DR with DME	3.5%
DR without DME	4.3%
ME from CRVO	1.6%
ME from BRVO	2.6%
Retinal Detachment	14.4%
Posterior uveitis	81.1%
Panuveitis	14.6%

Abbreviations: DR, diabetic retinopathy; DME, diabetic macular edema; ME, macular edema; CRVO, central retinal vein occlusion; BRVO, branch retinal vein occlusion

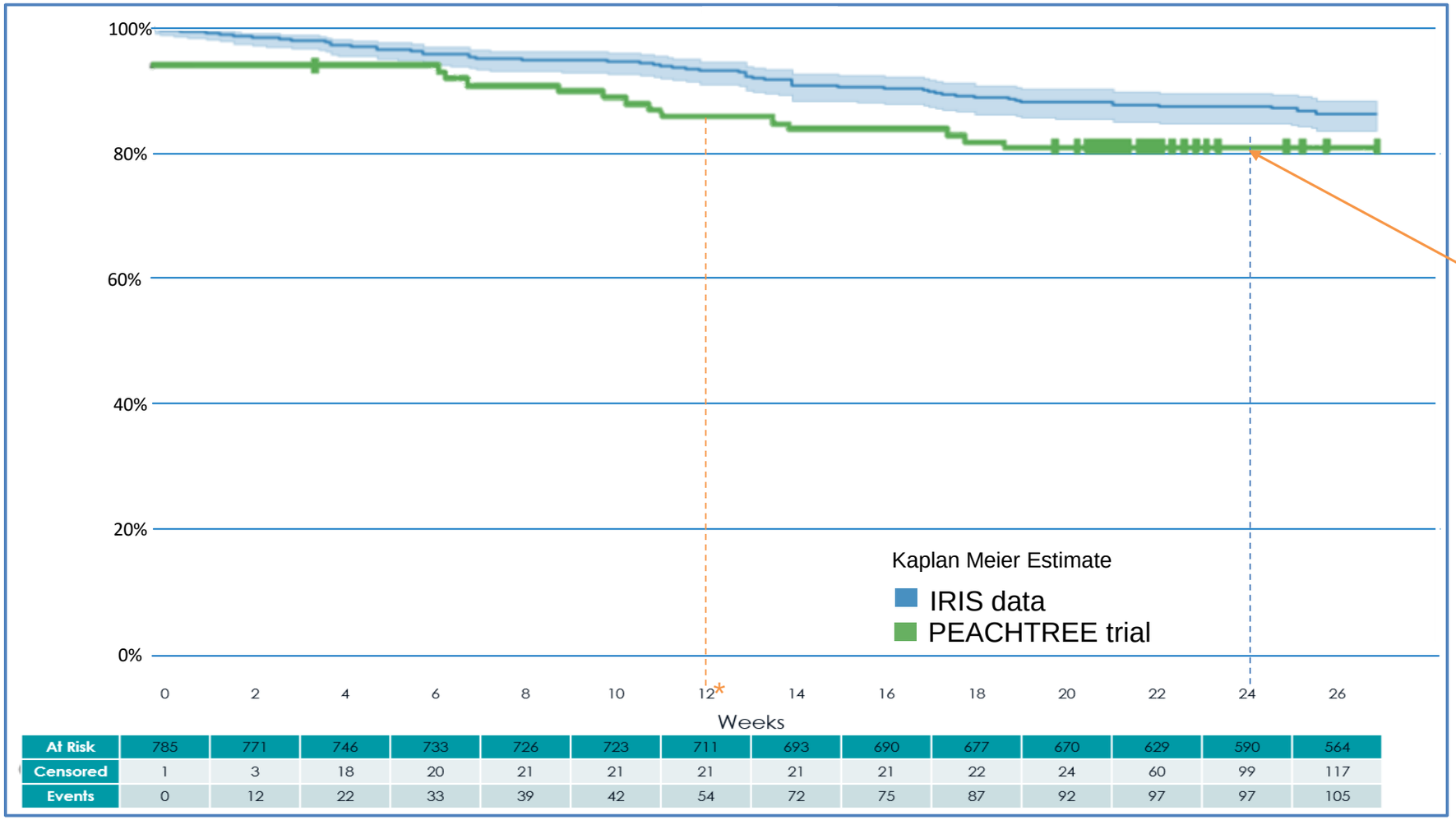
Treating provider subspecialty	
Retina/Vitreous Specialist	86.3%
Cataract/Anterior Segment Specialist	5.9%
Other/Unknown	7.9%

Prior corticosteroid use*	
Injectable/implantable with or without topical	35.2%
Topical only	17.3%

* This was only evaluated in the 786 patients whose data could be linked to claims

41.8% of patients had glaucoma or ocular hypertension prior to suprachoroidal triamcinolone injection

Time to rescue with injectable / implantable corticosteroid



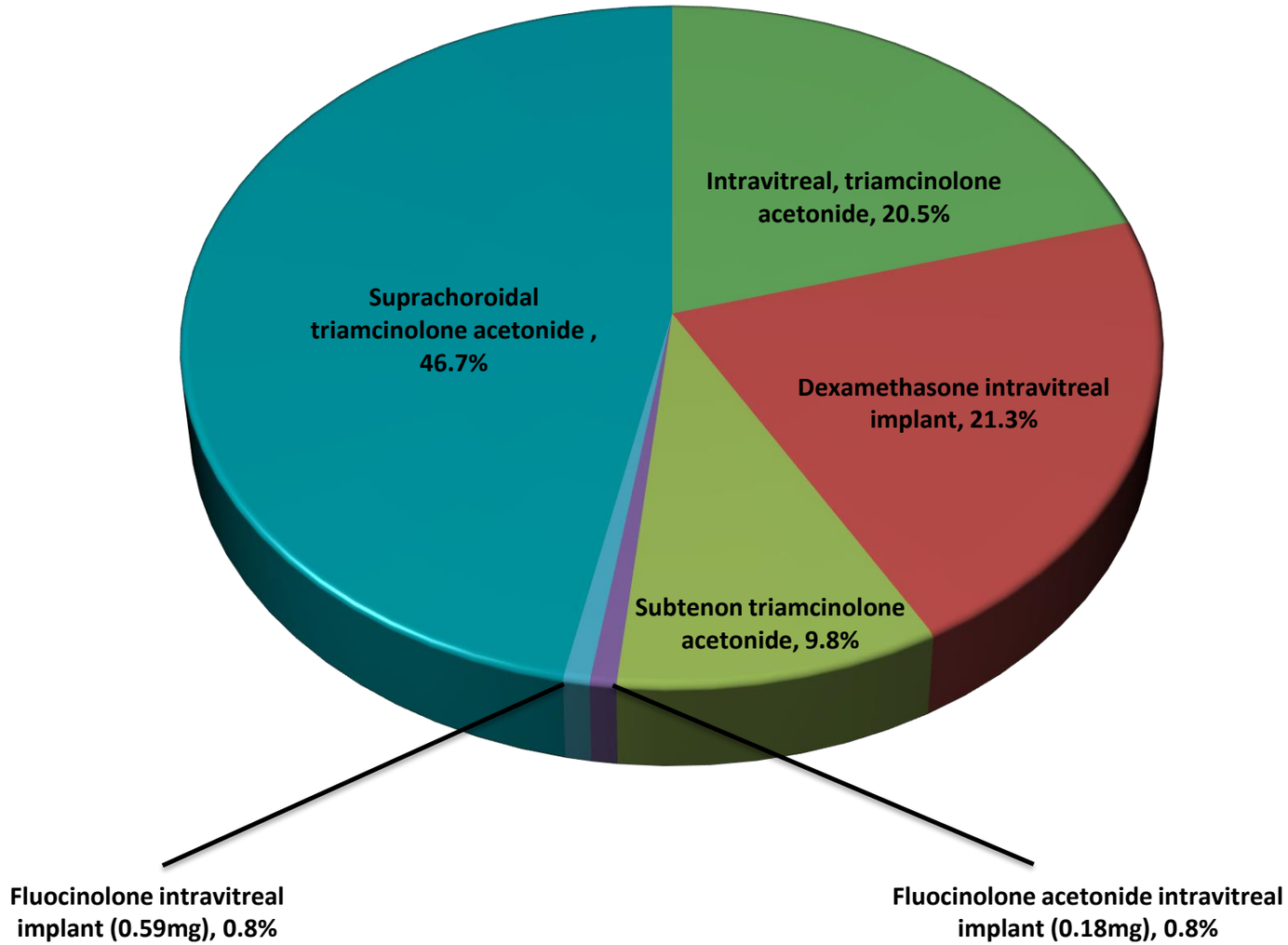
At Risk	785	771	746	733	726	723	711	693	690	677	670	629	590	564
Censored	1	3	18	20	21	21	21	21	21	22	24	60	99	117
Events	0	12	22	33	39	42	54	72	75	87	92	97	97	105

In PEACHTREE 86.5% did not require rescue therapy by week 24

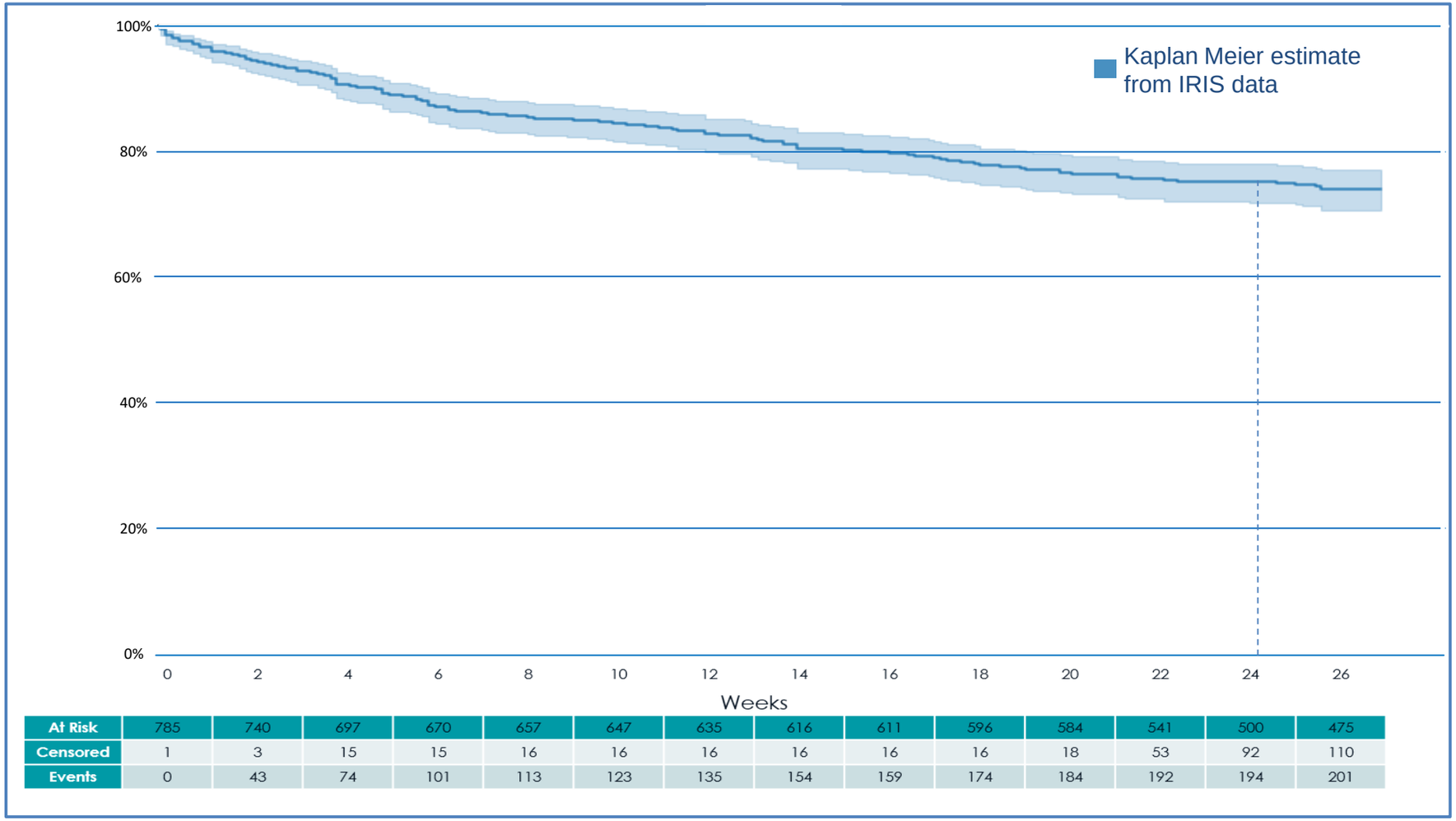
*In PEACHTREE, all subjects had a second injection at week 12

87.7% of eyes did not require an injected or implanted corticosteroid by week 24

Types of injected / implanted rescue therapy



Time to rescue with any corticosteroid (including topical)



At Risk	785	740	697	670	657	647	635	616	611	596	584	541	500	475
Censored	1	3	15	15	16	16	16	16	16	16	18	53	92	110
Events	0	43	74	101	113	123	135	154	159	174	184	192	194	201

75.4% of eyes did not require any corticosteroid by week 24

Patient considerations for suprachoroidal injections

Patient Selection

- High myopia or axial length
- Known scleral thinning
- History of glaucoma or hypotony
- History of ocular surgery

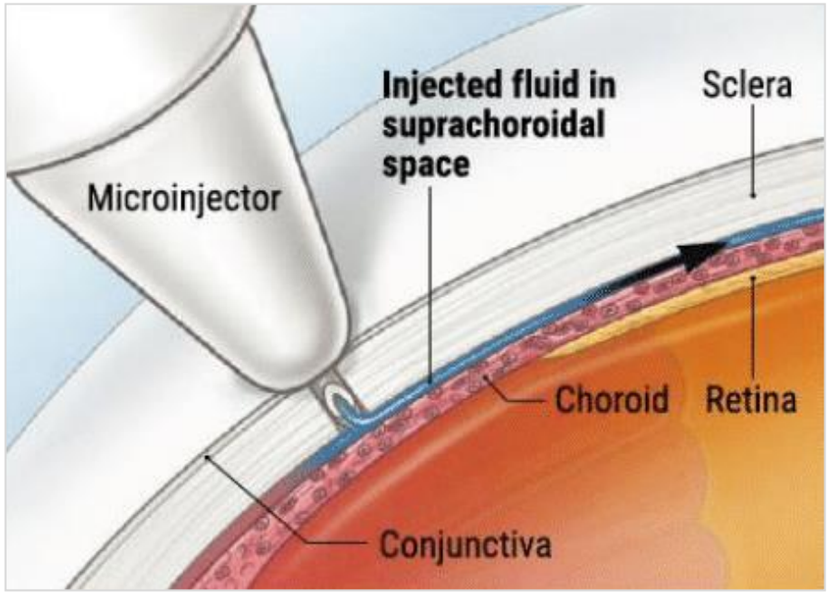
(esp. trabeculectomy or glaucoma shunt)

Patient Expectations

- Sensation of “pressure wave”
- Longer duration of procedure
- Possible change in needle or injection site

Patient Preparation

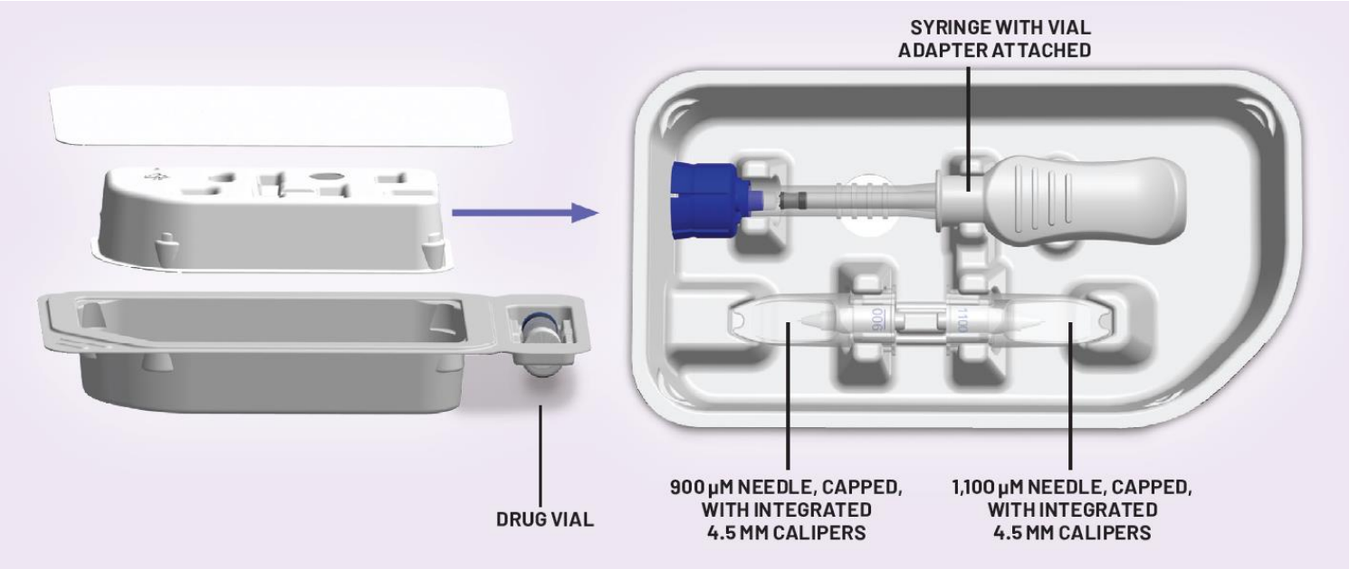
- Patient in supine position with head support
- Topical or subconjunctival anesthetic
- Povidone-iodine antiseptic
- Lid speculum recommended



Wykoff CC, Avery RL, Barakat MR, Boyer DS, Brown DM, Brucker AJ, Cunningham ET, Heier JS, Holekamp NM, Kaiser PK, Khanani AM, Kim JE, Demirci H, Regillo CD, Yiu G, Ciulla TA. Suprachoroidal Space Injection Technique: Expert Panel Guidance. Retina. (in press)

Images courtesy of Bausch & Lomb

Needle lengths & injection locations



Two needle lengths:
900 µm & **1,100 µm**

Preferred locations:
Superotemporal or
Inferotemporal

900µm needle + superotemporal quadrant
is **78% successful** on first attempt

Images courtesy of Bausch & Lomb

Suprachoroidal injection technique

RETINA
THE JOURNAL OF RETINAL AND VITREOUS DISEASES

REVIEW

SUPRACHOROIDAL SPACE INJECTION TECHNIQUE

Expert Panel Guidance

Wykoff, Charles C. MD, PhD*; Avery, Robert L. MD†; Barakat, Mark R. MD‡,§; Boyer, David S. MD¶; Brown, David M. MD*; Brucker, Alexander J. MD**; Cunningham, Emmett T. Jr MD, PhD, MPH††,‡‡,§§,¶¶; Heier, Jeffrey S. MD***; Holekamp, Nancy M. MD†††,‡‡‡; Kaiser, Peter K. MD§§§; Khanani, Arshad M. MD, MA¶¶¶,****; Kim, Judy E. MD††††; Demirci, Hakan MD‡‡‡‡; Regillo, Carl D. MD§§§§; Yiu, Glenn C. MD, PhD¶¶¶¶; Ciulla, Thomas A. MD, MBA*****

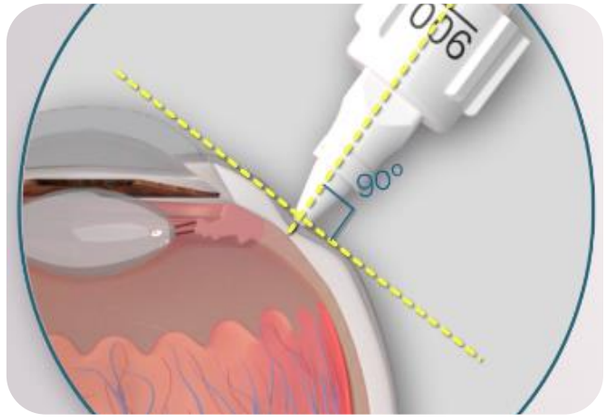
RETINA SPECIALIST

A beginner's guide to suprachoroidal injections

They require a different skill set than intravitreal injections. Here's a description of the technique.

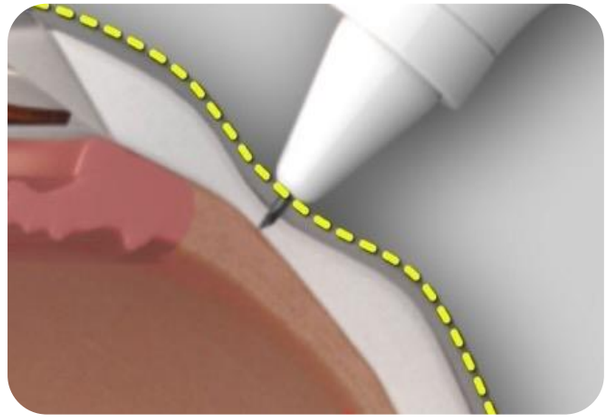
By Carol Villafuerte-Trisolini, MD, and Glenn Yiu, MD, PhD

DECEMBER 23, 2023



Perpendicular

Hold the microinjector **perpendicular** to the ocular surface



Dimple

Ensure firm contact with sclera by maintaining a **dimple** throughout injection

Slow

Inject **slowly** over 5 – 10 seconds

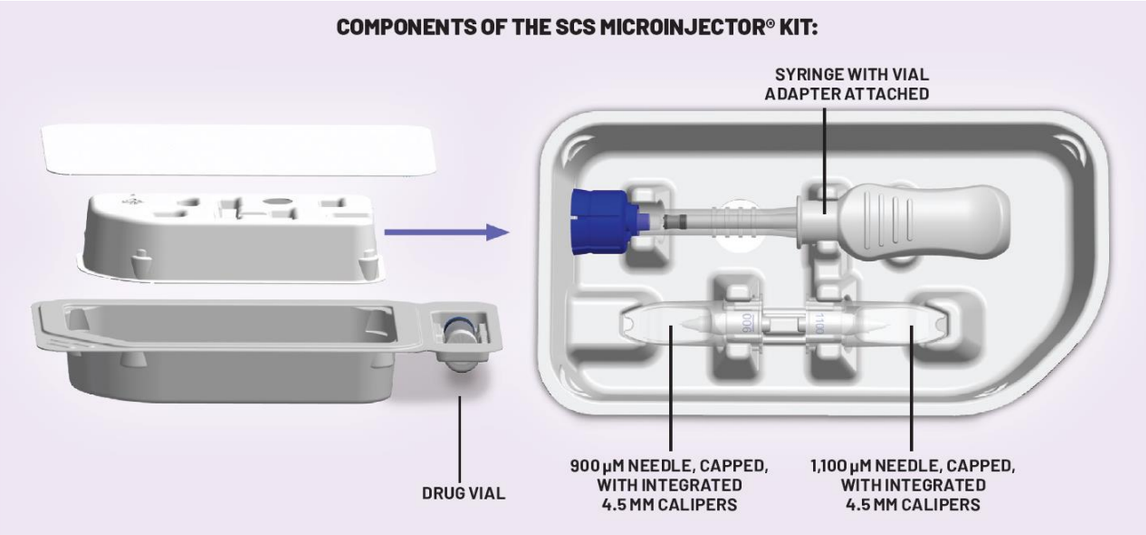
Images courtesy of Bausch & Lomb

Suprachoroidal drug / gene delivery in development

THERAPEUTIC	TYPE	INDICATION	IND-ENABLING	PHASE 1	PHASE 2	PHASE 3	APPROVAL
CLS-AX (axitinib):	**Tyrosine Kinase Inhibitor**	**Wet AMD**			Phase 2b		
XIPERE®	Corticosteroid *(Triamcinolone Acetonide)*	Uveitic Macular Edema *(U.S. & Canada)*					
XIPERE® / ARCATUS™	Corticosteroid *(Triamcinolone Acetonide)*	Uveitic Macular Edema Diabetic Macular Edema *(Asia Pacific ex-Japan)*				UME	
XIPERE® / ARCATUS™	Corticosteroid *(Triamcinolone Acetonide)*				DME		
Bel-Sar	Viral-like Drug Conjugate	Choroidal Melanoma				CoMpass	
ABBV-RGX-314	AAV Gene Therapy	Diabetic Retinopathy (DR)			ALTITUDE		
ABBV-RGX-314	AAV Gene Therapy	Wet AMD			AAVIATE		
Avoralstat	Plasma Kallikrein Inhibitor	Diabetic Macular Edema (DME)					

Image courtesy of Clearside Biomedical

Suprachoroidal drug delivery in the real world



CONCLUSIONS

- **Suprachoroidal microinjectors enable targeted delivery to the SCS, and suprachoroidal triamcinolone acetonide is FDA-approved for uveitic macular edema**

- **Durability of suprachoroidal triamcinolone in the real-world is comparable to phase 3 trial results, with ~12% needing subsequent corticosteroid within 24 weeks**

- **Optimal technique for suprachoroidal injections should be perpendicular, dimpling the sclera, and performed slowly**

Images courtesy of Bausch & Lomb