Front-line Local Therapies for Uveitis: *From Clinical Trials to Practice*

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Angiogenesis, Exudation and Degeneration 2020
17th Annual Meeting
Miami, Florida
February 8th, 2020

Financial Disclosures

Clearside Biomedical (Consultant, Grant)

Santen (Consultant, Advisory Board, Grant)

National Institutes of Health (Grant)

Research to Prevent Blindness (Grant)

Bayer Global Ophthalmology Awards Program (Grant)

Overview

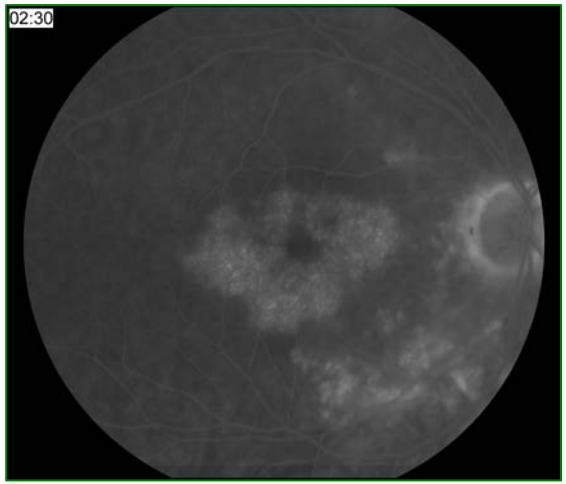
- Multicenter Uveitis Steroid Treatment Trial (MUST Trial - Fluocinolone acetonide vs. Systemic Immunosuppression)
- POINT Study – Ozurdex vs. Triamcinolone vs. Periocular Corticosteroid
- Fluocinolone acetonide insert (Yutiq)
- Suprachoroidal drug delivery (Xipere)
- Anti-VEGF therapy

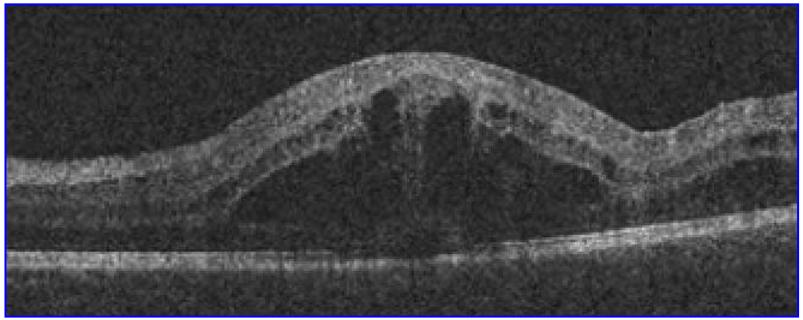
Macular Edema: A Structural Complication of Uveitis

Macular edema is the leading cause of vision impairment in uveitis

Therapeutic options for ME

- Local corticosteroid injections and topical eye drops
- Systemic immunosuppression
- Other local therapies
  - Anti-VEGF
  - Methotrexate
  - Sirolimus





1. Karim et al; Clin Ophthalmol. 2013;7:1109
2. Dick AD; *Br J Ophthalmol*. 1994;78:1
3. Lardenoye CWTA et al. *Ophthalmology*. 2006;113(8):1446

Multicenter Uveitis Steroid Treatment (MUST) Study

- Comparative efficacy trial assessing efficacy and safety of standard-of-care systemic immunosuppression vs. FA implant (Retisert)
- 0.59 mg implant, requiring surgery
- Risk of drug core dislocation, single-piece device now available

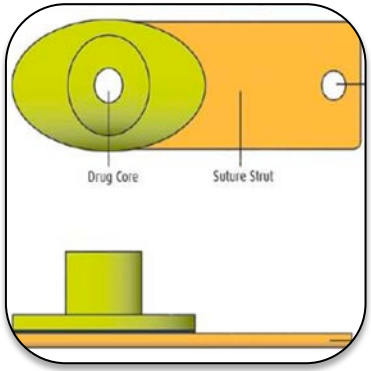
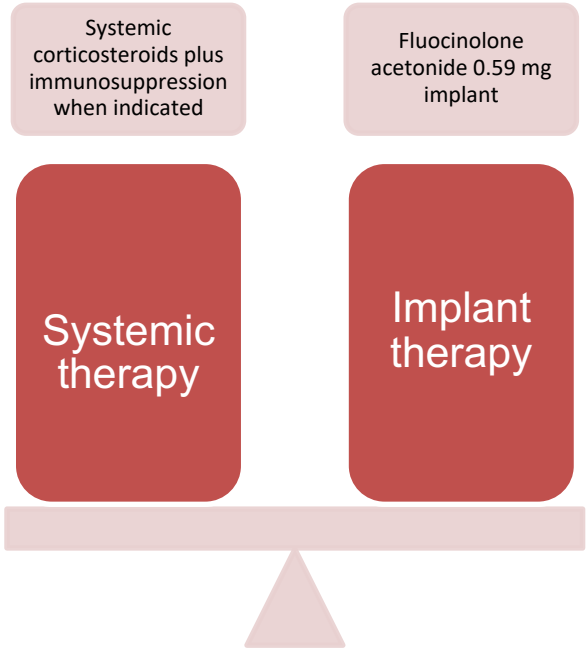


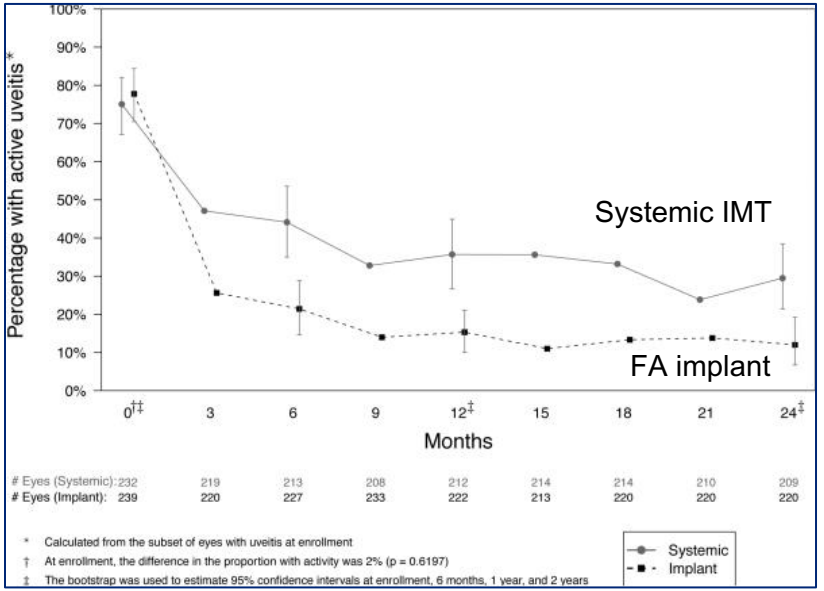
Photo Credit Dr. Thomas Albini



Multicenter Uveitis Steroid Treatment (MUST) Study

- **Corticosteroids plus systemic IMT vs. fluocinolone acetonide implant for NIU**
- **Efficacy**
  - Visual acuity improvements comparable between systemic and FA implant
  - Residual active inflammation favored implant vs. systemic IMT (12% to 29%)
- **Safety**
  - Higher rates of cataract (80%) and glaucoma (17%) in implant group
  - Higher rate of prescription-requiring infections in systemic IMT group

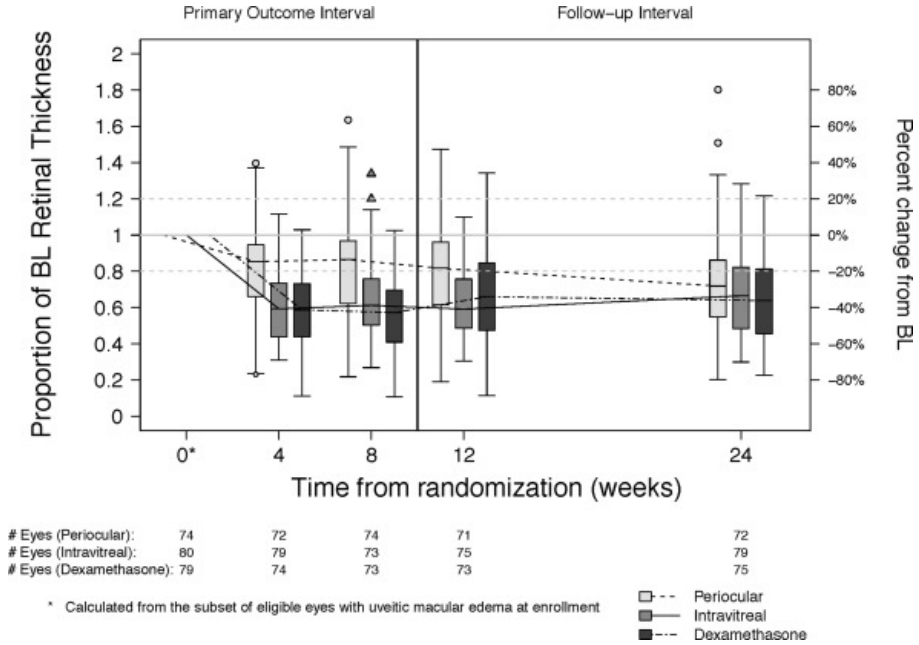
Percentage with active uveitis



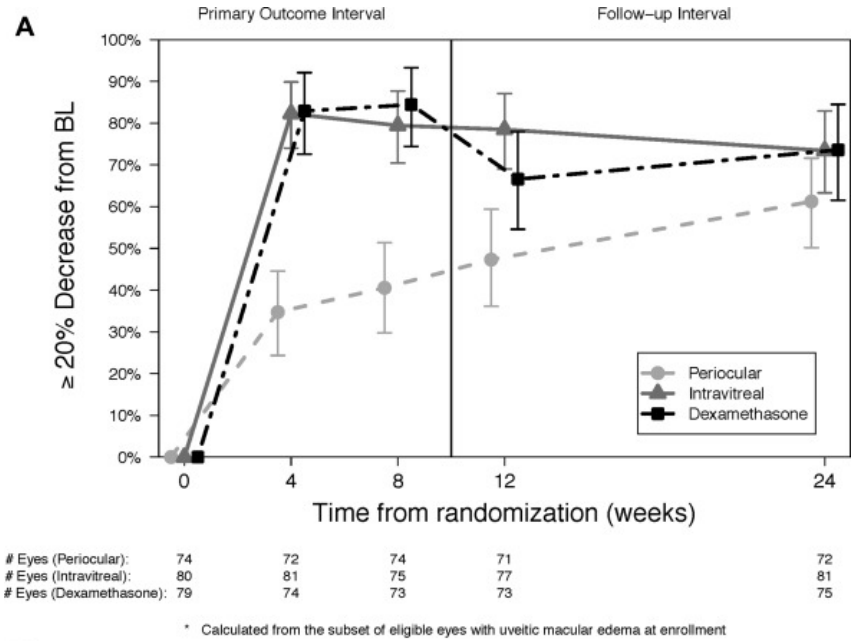
Ophthalmology 2011

The Periocular vs. Intravitreal corticosteroids for uveitic macular edema (POINT) Trial

% Baseline Retinal Thickness



20% Reduction in Baseline Retinal Thickness



Triamcinolone = Ozurdex > Periocular for Both Metrics

Multicenter Uveitis Steroid Treatment Trial Research Group; Writing Committee:, Periocular Triamcinolone vs. Intravitreal Triamcinolone vs. Intravitreal Dexamethasone Implant for the Treatment of Uveitic Macular Edema: The PeriOcular vs. INTravitreal corticosteroids for uveiticmacular edema (POINT) Trial. Ophthalmology. 2019;126(2):283-295.

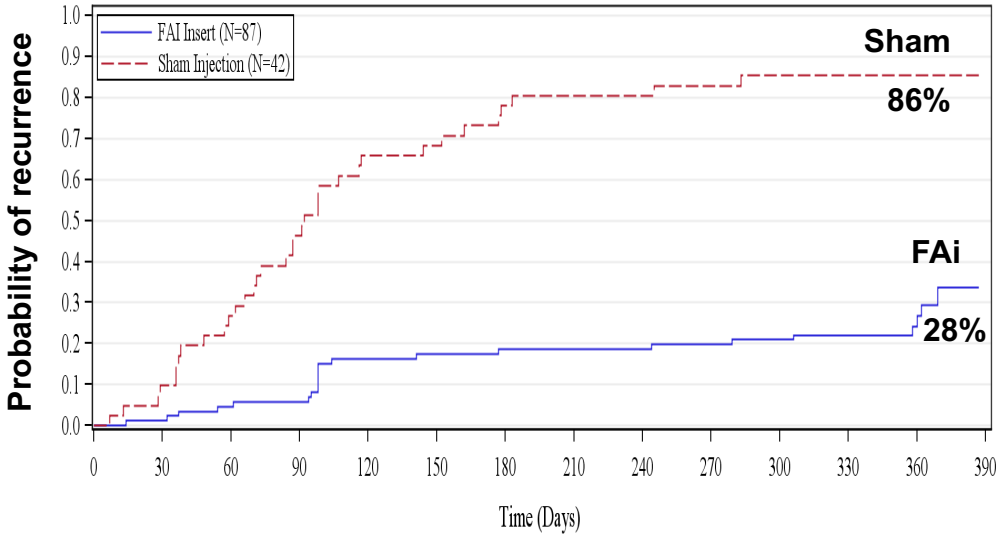
Fluocinolone Acetonide Intravitreal Microinsert 0.18 (FAi), 36-month drug delivery

- Rod-shaped, non-bioerodible device
- 25-gauge injector
- Two multicenter RCTs, randomized 2:1, FAi vs. Sham
  - PSV-FAi-001 – Multinational trial
  - PSV-FAi-005 - Multisites (India)
  - Primary endpoint: % patients requiring rescue within 6 months

Yutiq™ Full Prescribing Information, www.yutiq.com

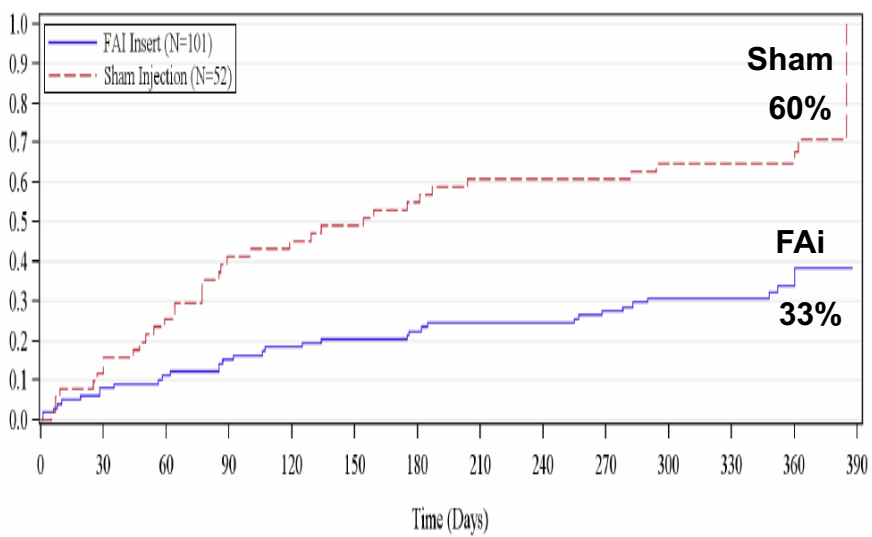
Fluocinolone Acetonide Intravitreal Insert for Macular Edema due to Noninfectious Uveitis

Study 001



- Reduced rate of vision loss
- Reduced need for adjunctive treatment in FAi

Study 005

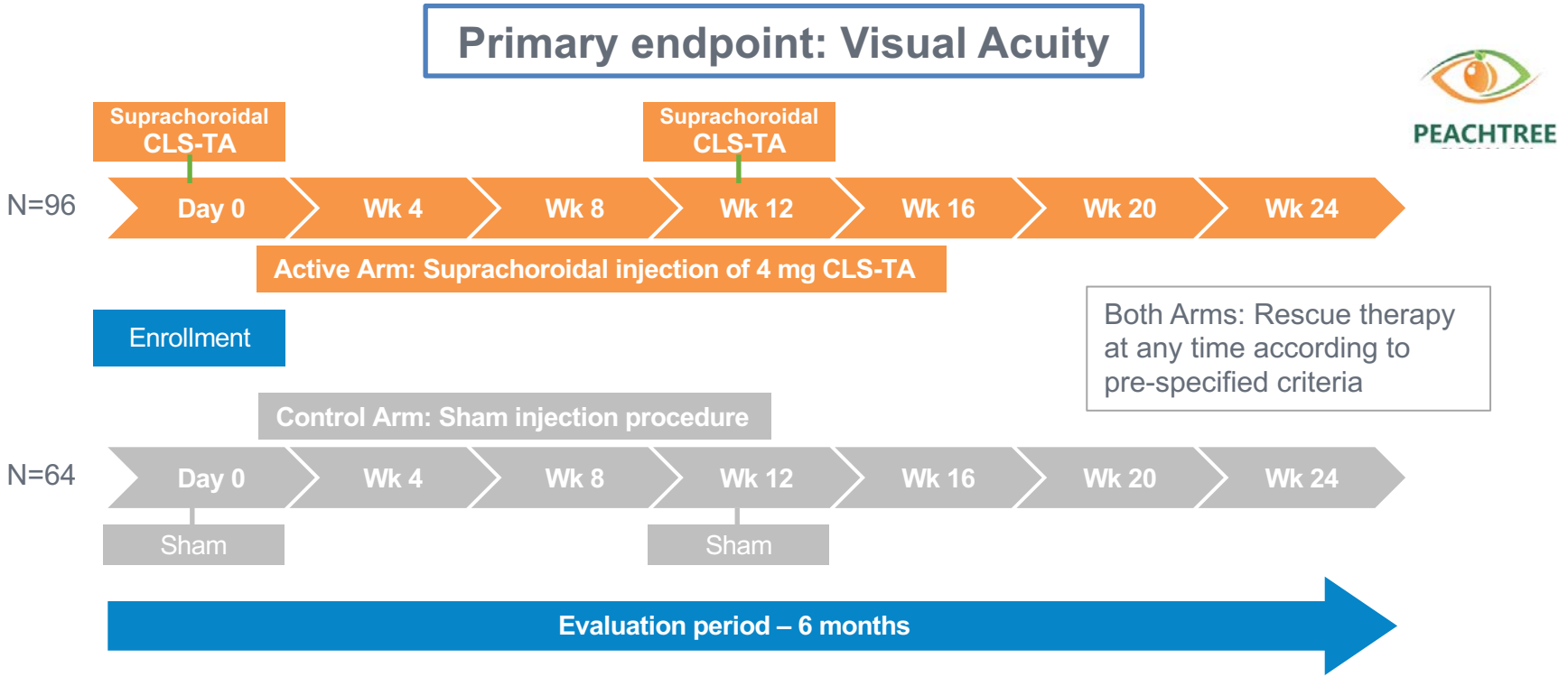


- Cataract requiring surgery: 33% in FAi; 5% in sham
- IOP-lowering medications: 26% in FAi and in sham

Jaffe et al, *Ophthalmology* 2019

Suprachoroidal Injection with the SCS Microinjector™

PEACHTREE: Phase 3, Randomized, Controlled, Double-Masked, Multicenter Trial

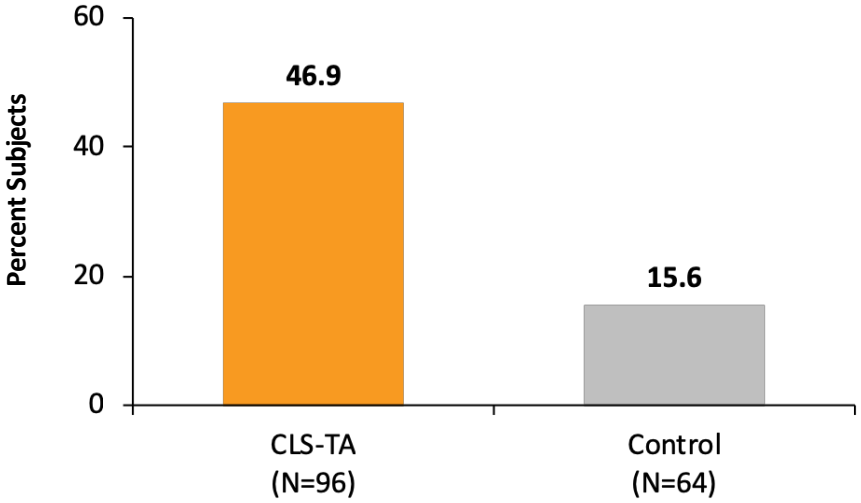


PEACHTREE Study Investigators, *Ophthalmol 2020*

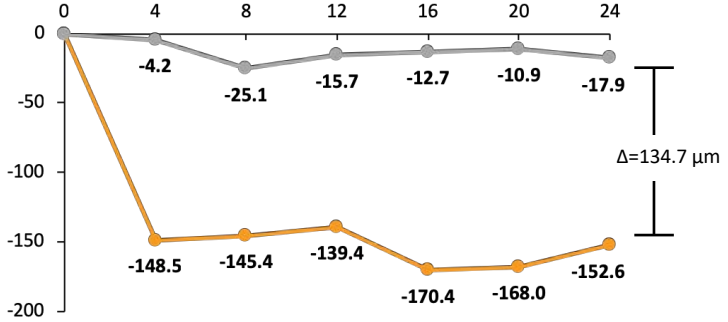
PEACHTREE Met Its Primary Efficacy Endpoint

Subjects gaining > 15 ETDRS letters, %

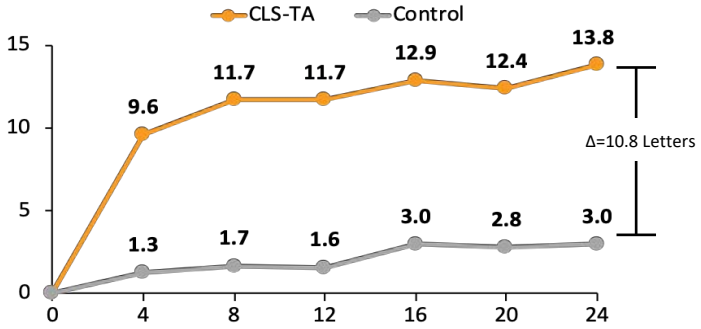
p<0.001 for comparison



Mean Change in CST



Mean Change in ETDRS BCVA



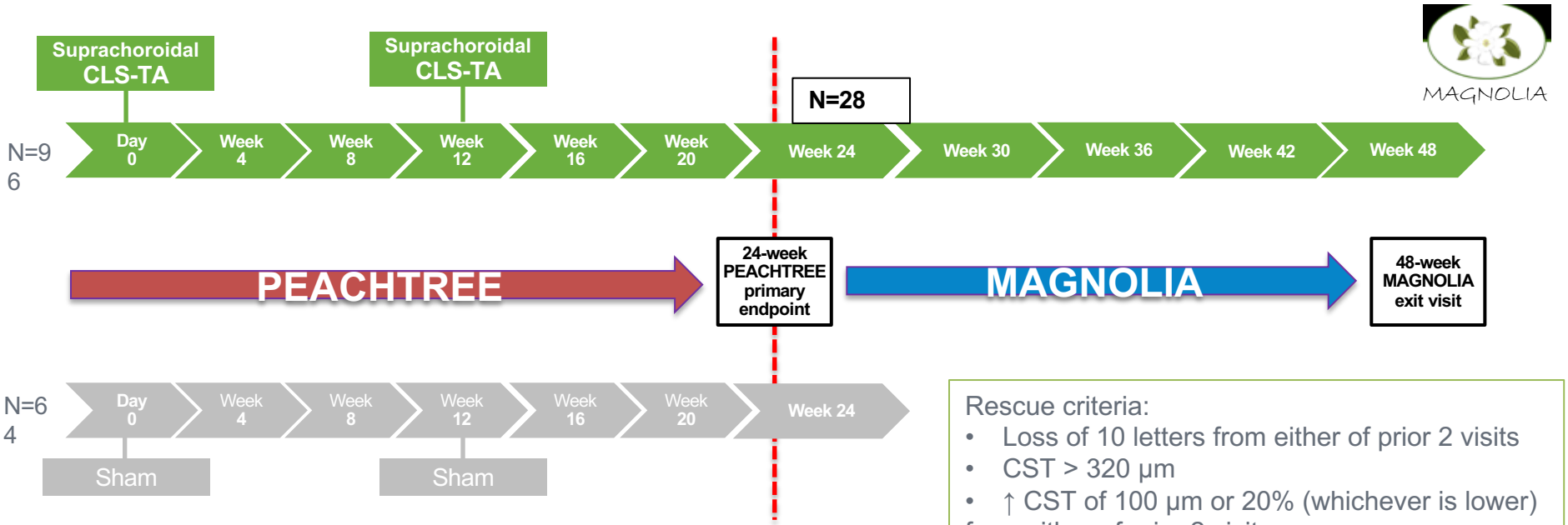
Intention-to-treat population; LOCF imputation.

The *p*-value is based on a CMH Cochran-Mantel-Haenszel test for general association between treatment and response with stratification by country.

ETDRS, Early treatment diabetic retinopathy study; LOCF, last observation carried forward.

MAGNOLIA: Prospective, Non-interventional, Masked, Observational 24-week Extension Trial

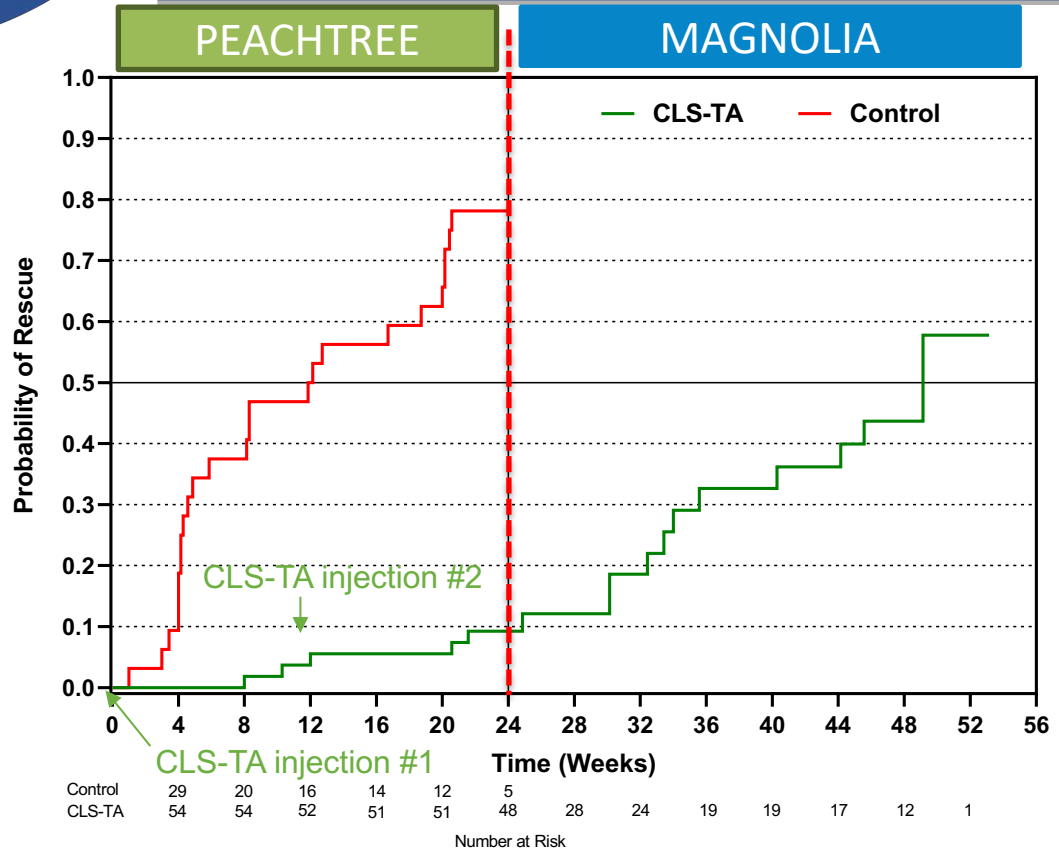
- To be eligible for MAGNOLIA, subjects must have completed PEACHTREE and **NOT** have received rescue medication
- Primary Endpoint: Time to rescue therapy relative to Day 0 of PEACHTREE



Rescue criteria:

- Loss of 10 letters from either of prior 2 visits
- CST > 320 µm
- ↑ CST of 100 µm or 20% (whichever is lower) from either of prior 2 visits
- Investigator discretion

Primary Endpoint:
Kaplan-Meier Plot Time to First Rescue



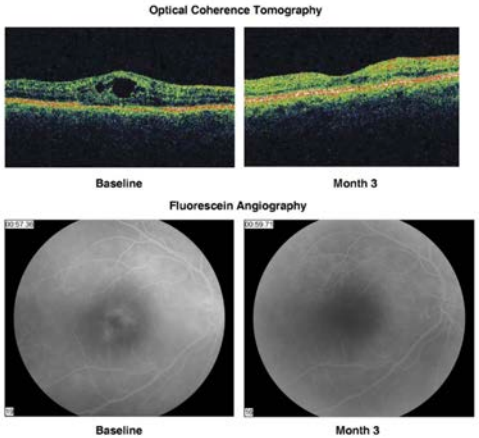
- **50% of CLS-TA subjects did not receive any additional medication through Week 48**
- **9 months from last CLS-TA dose**

No significant differences in baseline characteristics were seen between patients who enrolled in MAGNOLIA vs patients who were eligible to enroll in MAGNOLIA but didn't.

Anti-VEGF for macular edema due to NIU

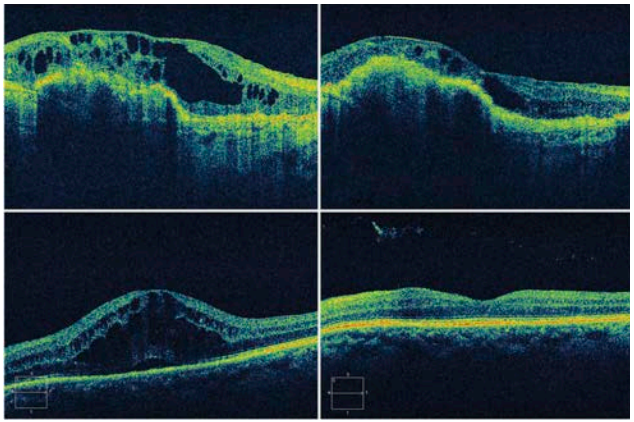
Ranibizumab (RZB) for ME
Acharya et al *AJO 2009*

- Monthly injections of RZB for ME due to NIU x 3 months
- 13-letter VA gain with OCT improvement
- Seven patients enrolled



Ranibizumab (RZB) for ME
Reddy et al *Retina 2014*

- OCT-guided RZB injections for ME due to NIU
- ~12-letter gain over time with OCT improvements over 12 months

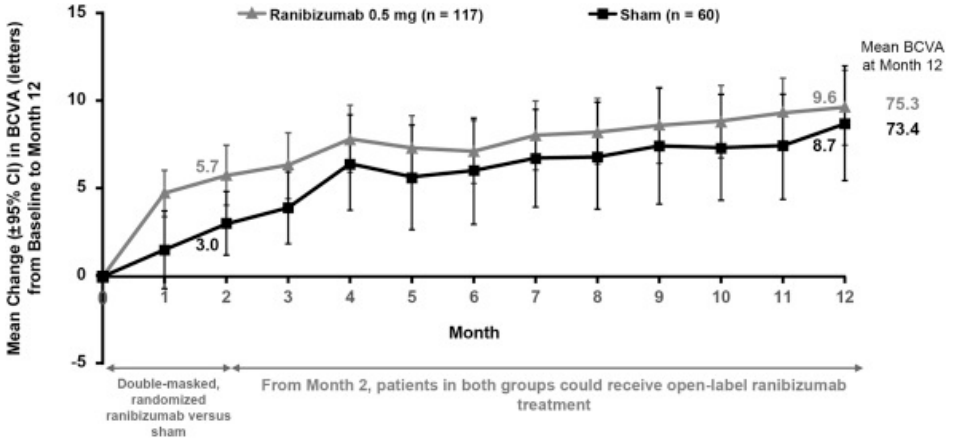


Anti-VEGF for macular edema due to NIU

Phase 3 RCT, sham controlled study, 178 pts randomized to 0.5 mg ranibizumab (n=110) 0.5 mg or sham (n=68) at month 0 and 1

- Open label at 2-months thereafter according to disease activity
- +5.8 letters (treatment), +2.9 in sham (p=0.011)

PROMETHEUS Study
Ranibizumab for ME due to 'uncommon causes'



Staurenghi et al *Ophthalmology 2018*

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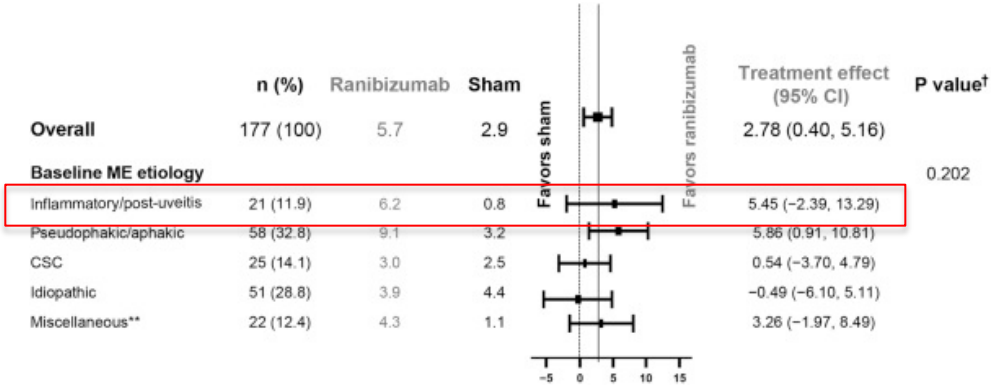
- Open label at 2-months thereafter according to disease activity
- +5.8 letters (treatment), +2.9 in sham (p=0.011)
- 21 patients randomized from the uveitis cohort

PROMETHEUS Study
Ranibizumab for ME due to 'uncommon causes'



Staurenghi et al *Ophthalmology 2018*

Summary

- Phase 3 studies have demonstrated the benefit of local corticosteroids via novel drug delivery platforms for macular edema due to noninfectious uveitis
- Other agents (ranibizumab, methotrexate, and sirolimus) remain under investigation for noninfectious uveitis
- Promising outlook for local delivery options for noninfectious uveitis