UVEITIS TREATMENT

PHYSICIAN LECTURE II

OBJECTIVES

Describe	Treatment options for uveitis
Delineate	Specifics steps to improve topical therapy outcomes
Describe	Current options for regional therapy for uveitic syndromes
Outline	Clinical approach to medical management for uveitis

CATEGORIES OF TREATMENT OPTIONS

LOCAL: Part I

- Topical
- Regional

SYSTEMIC: Medical

- Oral
- Subcutaneous
- Intravenous


YOU ARE ENTERING A DANGER ZONE
Top mistakes in using topical corticosteroids

FOCUS ON ANATOMICAL EFFICACY AND SAFETY

CONFIRM ANATOMICAL INVOLVEMENT

MONOTHERAPY vs COMBINATION THERAPY

STEROID RESPONSE

Early Evaluation

Timely Treatment

Monitor for Progression

CONFIRM STEROID RESPONSE vs UVEITIC GLAUCOMA

INFECTIOUS KERATITIS?!

Associated Stromal Keratitis

Soft Contact Lens Wearers

BEWARE OF THE MASQUERADE

Fuchs's Heterochromic Iridocyclitis

Glaucomatocyclitic Crisis (Posner-Schlossman Syndrome)

REGIONAL THERAPY FOR UVEITIS: KEY TAKE-AWAYS

REGIONAL THERAPEUTIC OPTIONS

PERIOCULAR

- Depot corticosteroids

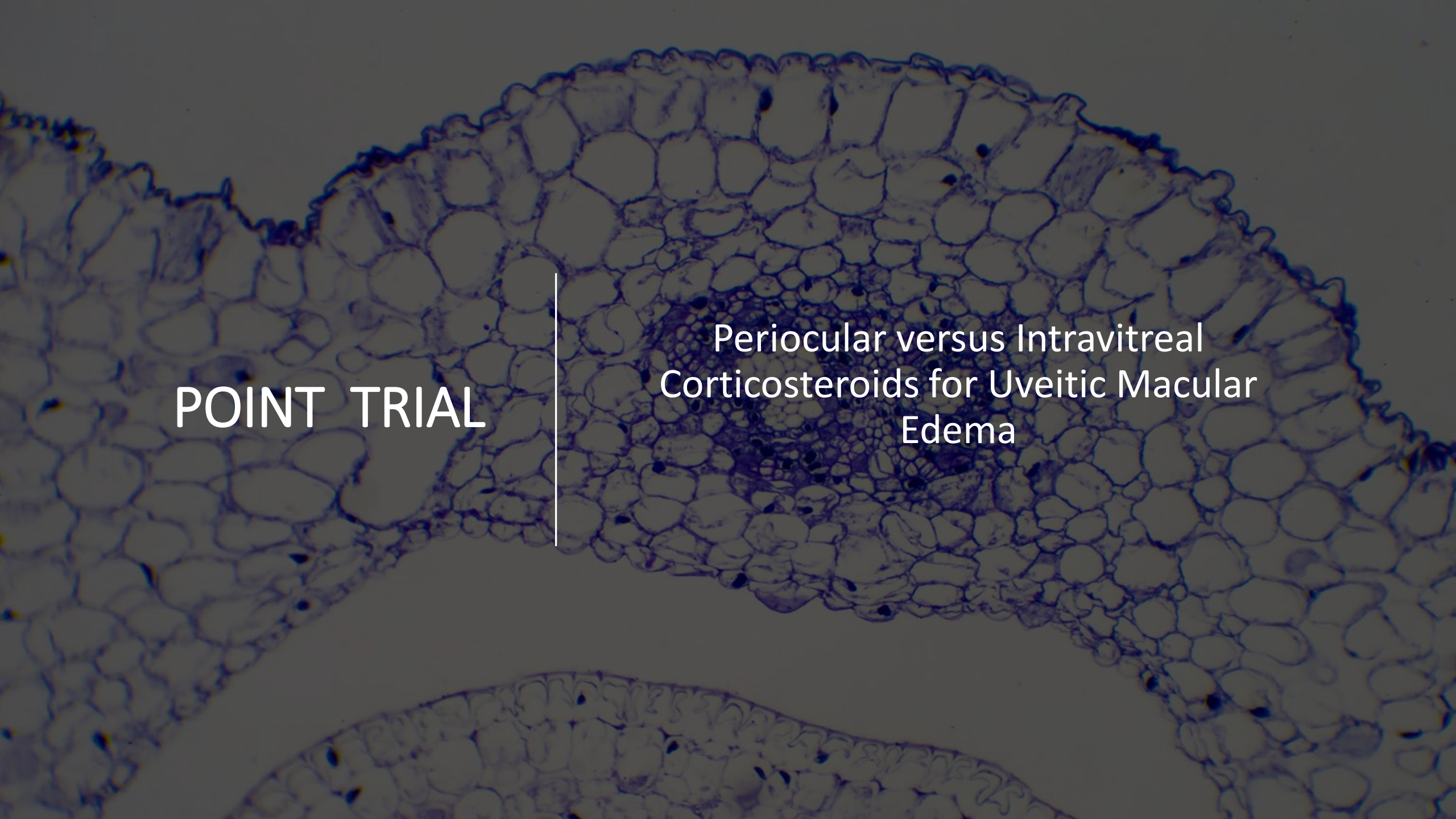
INTRAVITREAL

- Triamcinolone acetonide 40 mg/ml (TRIESENCE)

SUSTAINED-RELEASE CORTICOSTEROID IMPLANTS

- Surgically fixed to the sclera
  - Fluocinolone acetonide (Retisert 0.59 mg)
- Injected into the vitreous: Embedded to either a biodegradable or nonbiodegradable vehicle
  - Dexamethasone (Ozurdex 0.7 mg)
  - Fluocinolone acetonide (Yutiq 0.18 mg)

- **SUPRACHOROIDAL** route, XIPERE™ is 4 mg (0.1 mL of the 40 mg/mL)



POINT TRIAL

Periocular versus Intravitreal Corticosteroids for Uveitic Macular Edema

AIM

Compared the effectiveness of 3 different regional corticosteroid injections in eyes with uveitic (not pseudophakic) CME

4 mg of triamcinolone given intravitreally

0.7-mg dexamethasone intravitreal implant

40-mg periocular triamcinolone injection

RESULTS

- Intravitreal resulted in greater improvement in macular thickness at 8 weeks

TAKE AWAY/PRECAUTION

**Periocular injections had a lower risk of IOP elevation compared to the intravitreal

SYSTEMIC THERAPY

ESTABLISHED EXPERT RECOMMENDATIONS

Selected Diseases with Poor Natural History

CORTICOSTEROID SIDE-EFFECTS

- HYPERTENSION
- IMMUNOSUPPRESSION
- GASTRIC ULCERS
- HEARTBURN
- CATARACT
- OSTEOPOROSIS
- MUSCLE WEAKNESS
- PSYCHOSIS
- ACNE
- HYPERGLYCEMIA
- CUSHINGOID
- MYOPATHY
- POOR WOUND HEALING
- REDUCED STRESS RESPONSE

STEROIDS: SIX WEEKS LATER…..

CORTICOSTEROID-SPARING AGENTS

- Drug Class/Mechanism of Action
- Screening and Monitoring Protocol
- Most Common Side-effects

IMMUNOSUPPRESSIVE AGENTS

ANTI-METABOLITES	T-CELL INHIBITORS	ALKYLATING/CYTOTOXIC AGENTS	BIOLOGICS
METHOTREXATE	CYCLOSPORINE	CYCLOPHOSPHAMIDE	HUMIRA (ADALIMUMAB)
MYCOPHENOLATE MOFETIL (CELLCEPT)	TACROLIMUS	CHLORAMBUCIL	REMICADE (INFLIXIMAB)
AZATHIOPRINE (IMURAN)	RAPAMYCIN		RITUXAN (RITUXIMAB)
LEFLUNAMIDE (ARAVA)	DACLIZUMAB		ACTEMRA (TOCLIZUMAB)

BIOLOGICS

Systemic Immunosuppressive Therapy for Eye Disease

SITE

- Retrospective Cohort Study
- Past use of **immunosuppressive therapy**
- Approximately **9,250** ocular inflammation patients
- **Five** tertiary centers up to **30 years**
- **Initial publication in 2008/Currently 26 Publications**

SITE: GENERAL GUIDELINES

METHOTREXATE

Anterior Uveitis

CELLCEPT

MOST UVEIDITIES

MTX VS MMF

SITE:

- MMF may be faster than MTX in achieving corticosteroid-sparing success in ocular inflammatory diseases

FAST RESEARCH GROUP (Acharya; First-line Antimetabolites as Steroid-sparing Treatment (FAST) uveitis trial

- **MMF** as first-line corticosteroid-sparing treatment **did not result in superior control** of inflammation **VS MTX**
- Screened **265** adults from 9 referral eye centers in India, the United States, Australia, Saudi Arabia, and Mexico between August 22, 2013, and August 16, 2017

CYCLOSPORIN

Alternative agents may be preferred for patients aged more than **55 years**

3-fold more likely to discontinue therapy because of toxicity

AZATHIOPRINE

- Required several months to achieve treatment goals

CYCLOPHOSPHAMIDE

- Severe ocular inflammation cases where the potentially vision-saving benefits outweigh the substantial potential side effects of therapy
- Associated systemic inflammatory diseases

Levy-Clarke et al. Expert Panel Recommendations for the Use of anti-TNF Biologic Agents; Ophthalmology: (2014)

- Infliximab and adalimumab: # 1 **Behçet's disease**
- Infliximab and adalimumab: # 2 **Juvenile idiopathic arthritis**
- Infliximab and adalimumab: # 2
  - **Posterior uveitis, panuveitis**
  - Severe uveitis associated with **seronegative spondyloarthropathy**
  - **Scleritis**
  - **Etanercept, which seems to be associated with lower rates of treatment success**

HUMIRA: FDA APPROVED

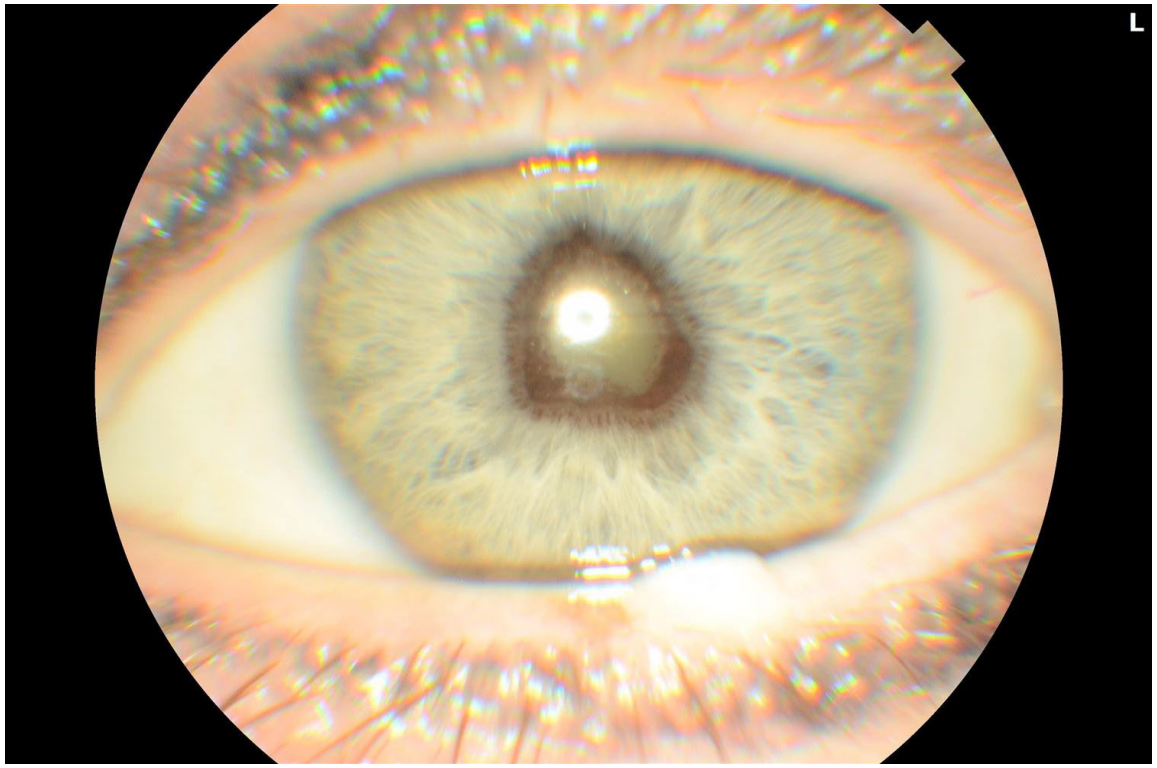
FDA approved 2016: Non-infectious, Intermediate, Posterior, Panuveitis

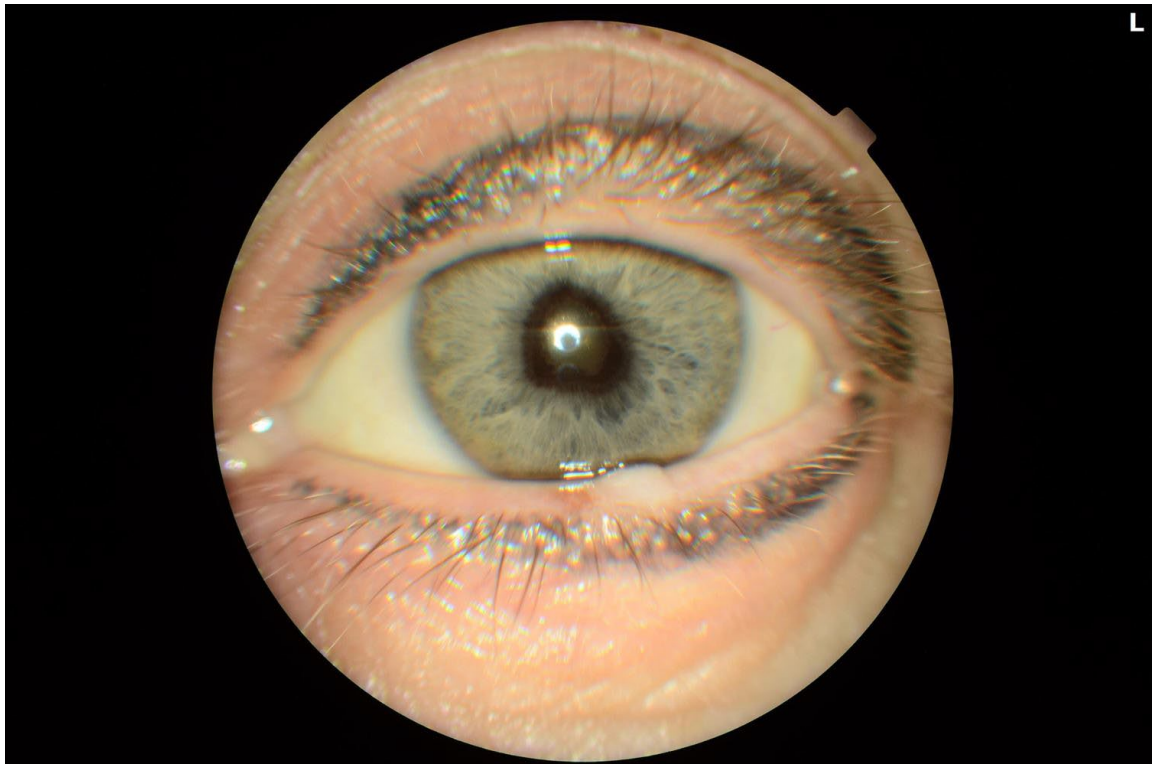
CLINICAL CASE

CHRONIC BILATERAL ANTERIOR UVEITIS

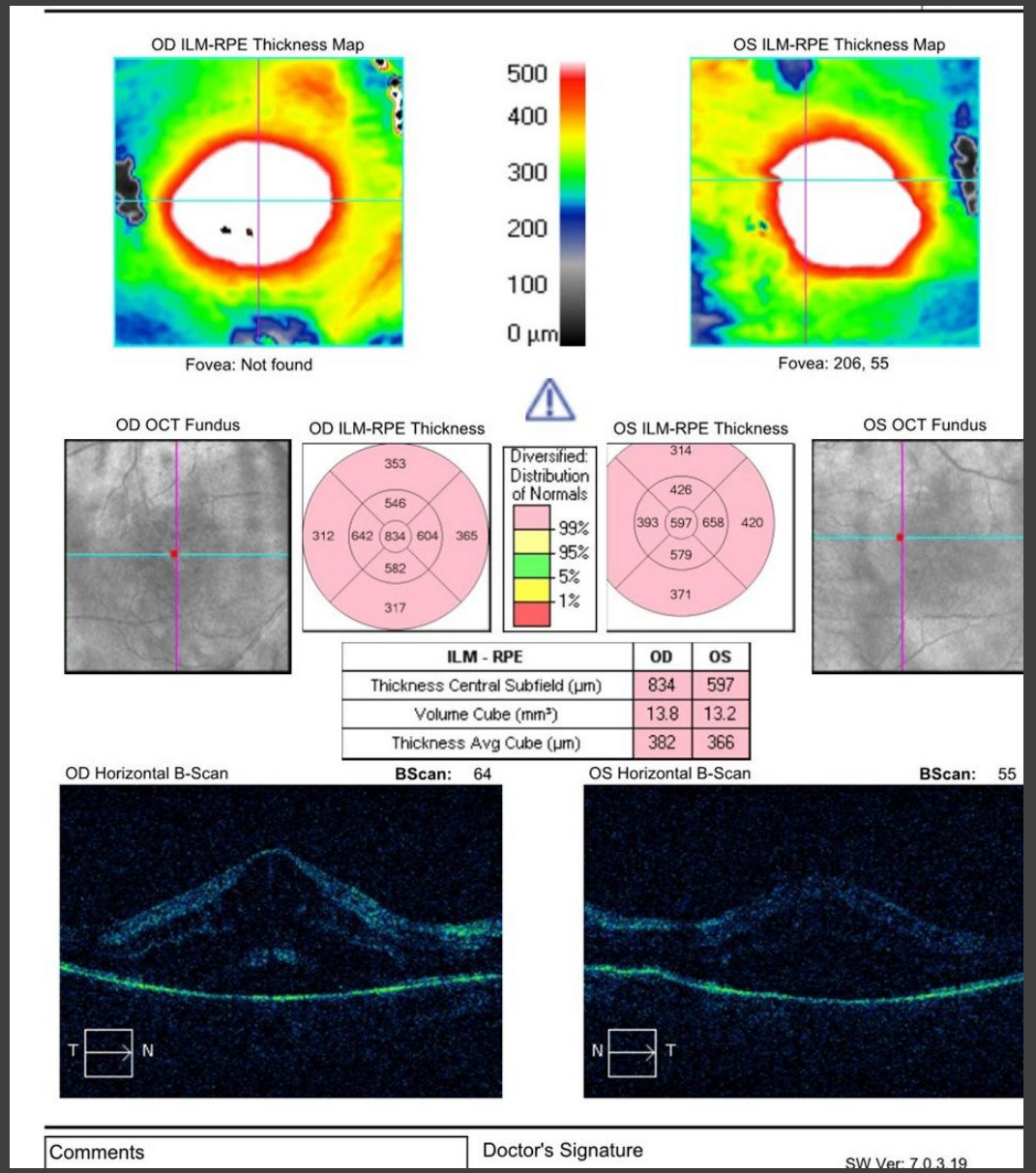
- 60-Year-old Caucasian Female
- Treated only with extended/protracted course of topical corticosteroids
- 20/80 & 20/60, normal IOP
- Psoriatic Arthritis
- Treated with Otezla/Apremilast (PDE4 inhibitor)
- H/O Malignant Melanoma
- Insulin Dependent Diabetic
- Osteoporosis

PERTINENT FINDINGS





INITIAL OCT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Fovea: Not found
Fovea: 206, 55
OD OCT Fundus
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Diversified: Distribution of Normals
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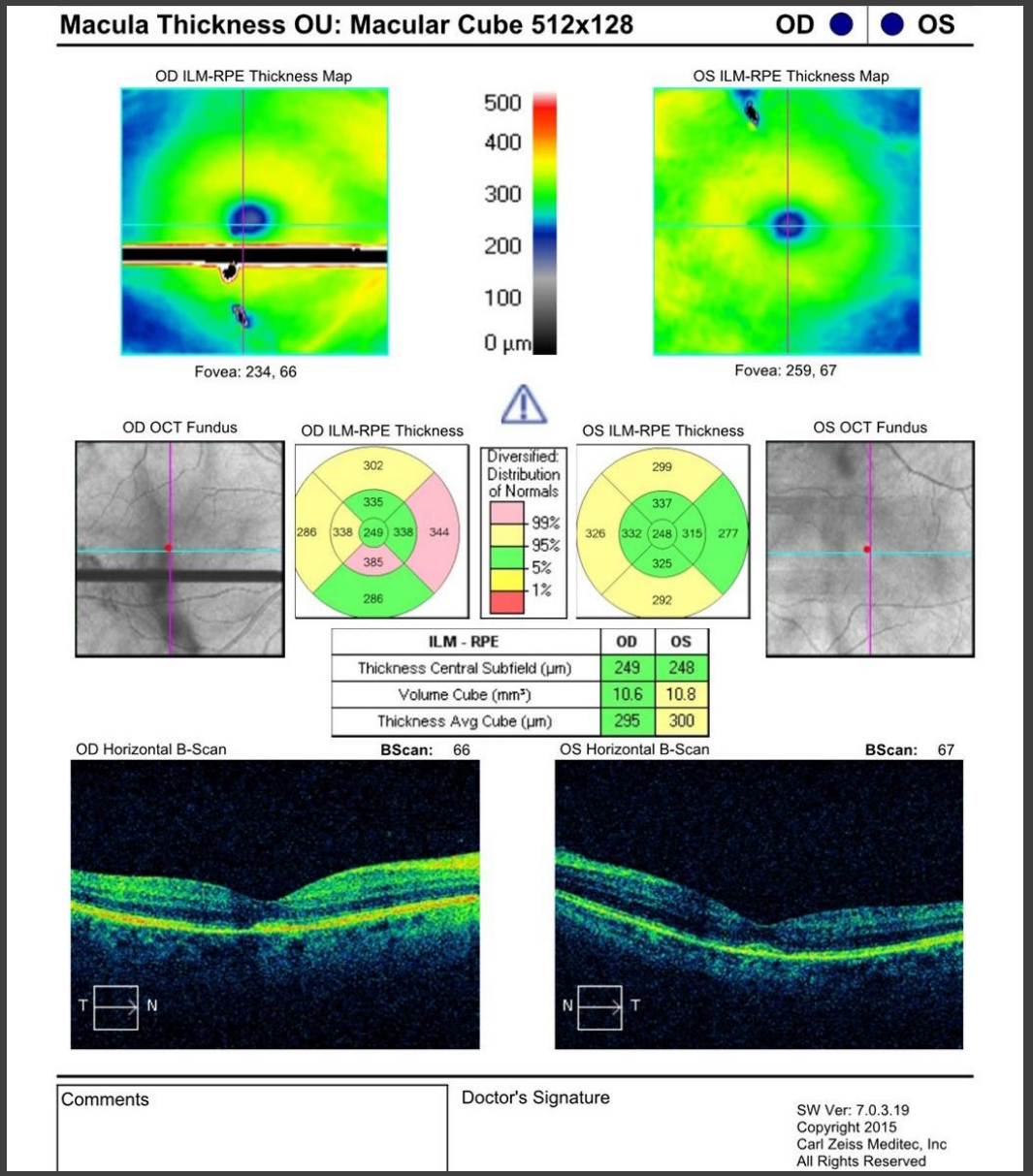
Doctor's Signature
SW Ver: 7.0.3.19

PRE-OP OCT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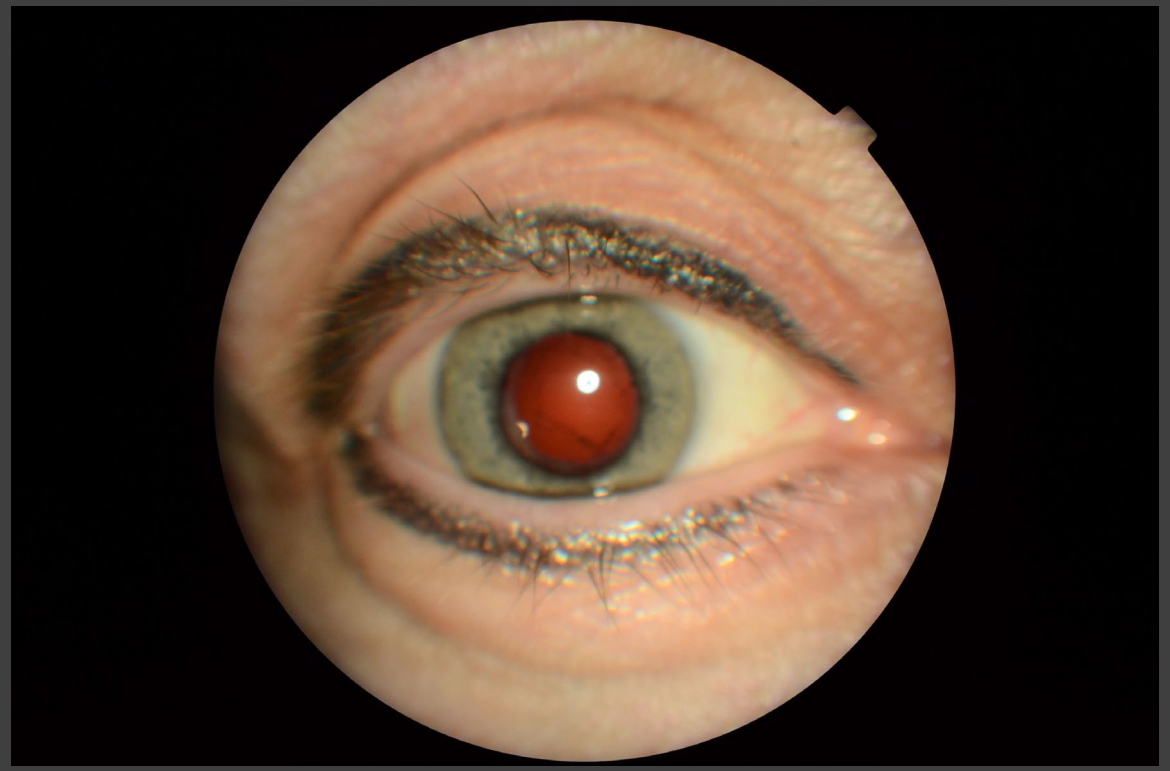
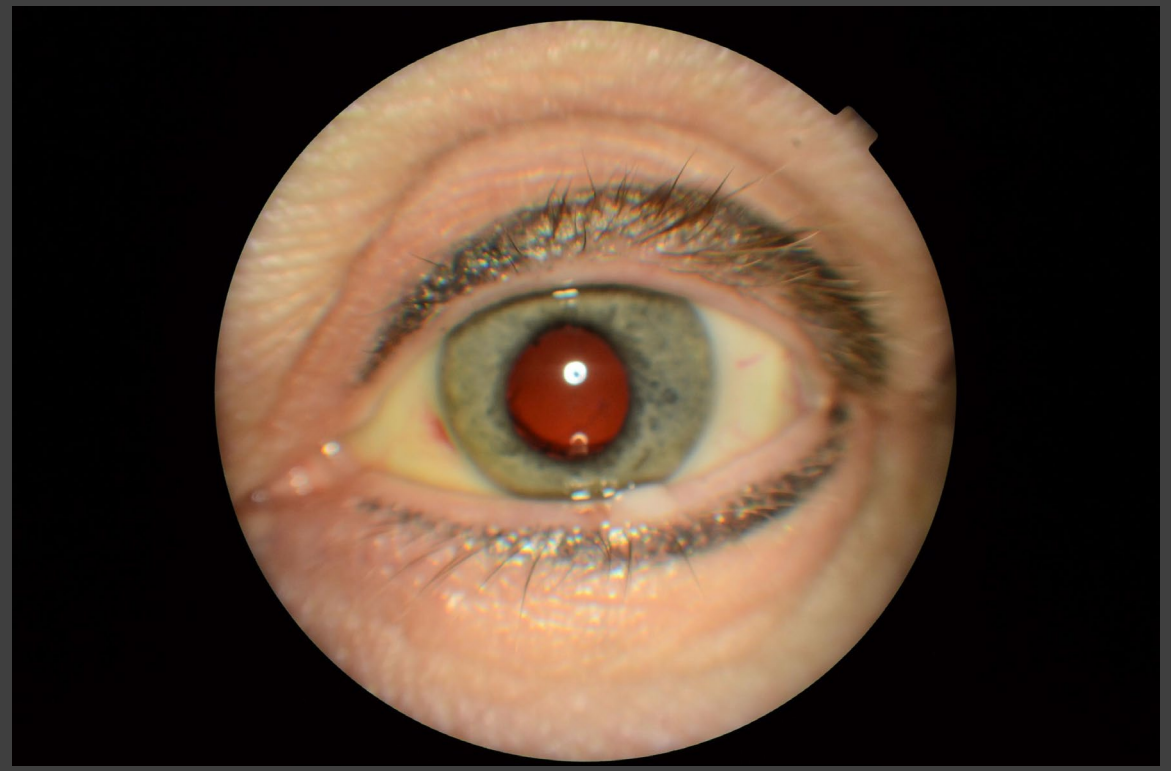
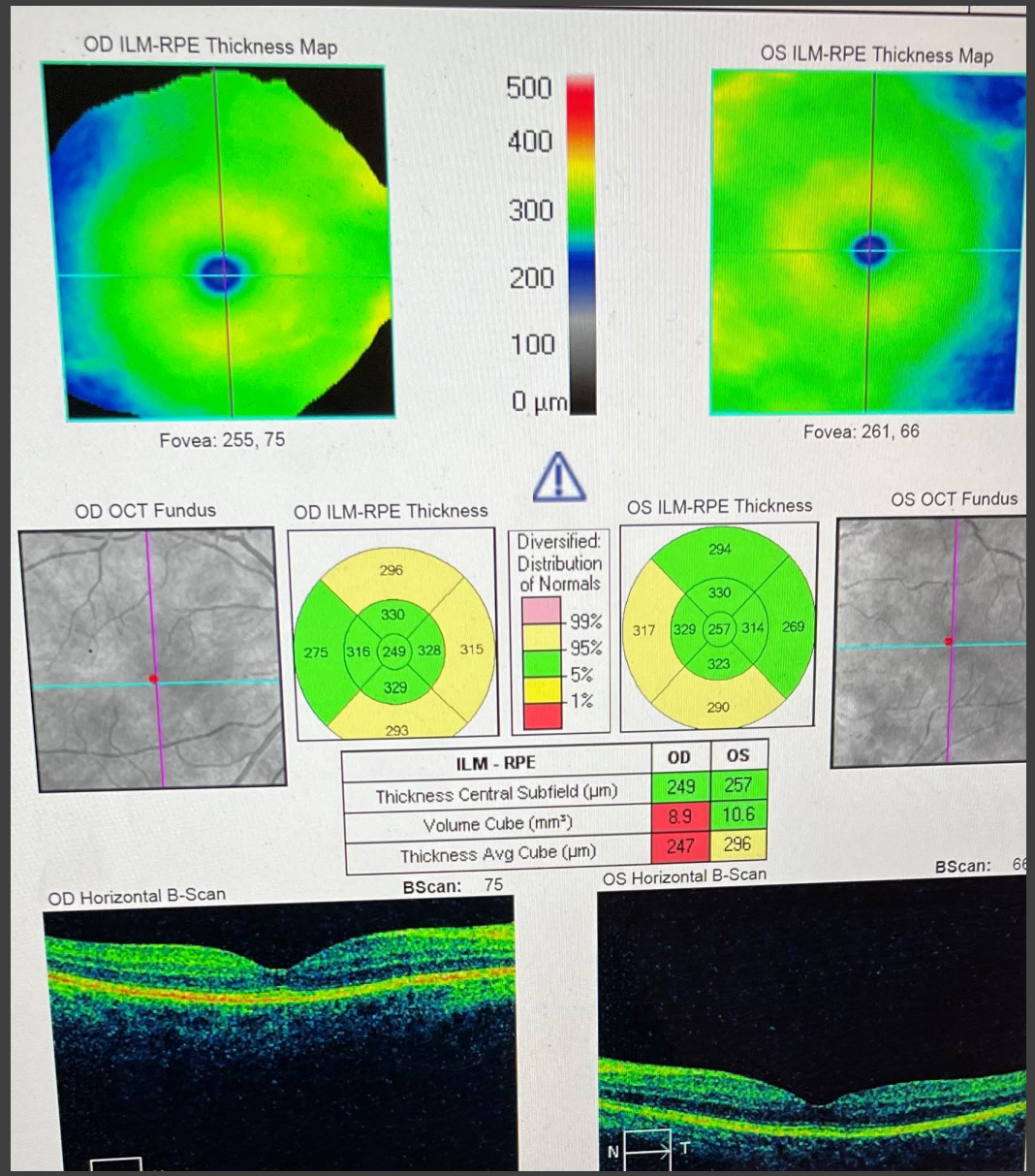




PSEUDOPHAKIC: S/P SYNECHIOLYSIS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N
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CURRENT OCT

REFERENCES

- 2019-2020 BCSC Complete eBook Set
- Thorne JE et al: Multicenter Uveitis Steroid Treatment Trial Research Group. Periocular Triamcinolone vs. Intravitreal Triamcinolone vs. Intravitreal Dexamethasone Implant for the Treatment of Uveitic Macular Edema: The PeriOcular vs. INTravitreal corticosteroids for uveitic macular edema (POINT) Trial. Ophthalmology. 2019 Feb;126(2):283-295. doi: 10.1016/j.ophtha.2018.08.021.
- Chu CJ, Dick AD, Johnston RL, Yang YC, Denniston AK; UK Pseudophakic Macular Edema Study Group. Cataract surgery in uveitis: a multicentre database study. Br J Ophthalmol. 2017 Aug;101(8):1132-1137.
- Focal Points 2020 Module: Management of Cataract Surgery and Uveitis
- Kempen JH, Daniel E, Gangaputra S, Dreger K, et al. Methods for identifying long-term adverse effects oftreatment in patients with eye diseases: the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Cohort Study. Ophthalmic Epidemiol. 2008 Jan-Feb;15(1):47-55