



STATE BOARD OF OPTOMETRY
 2450 DEL PASO ROAD, SUITE 105, SACRAMENTO, CA 95834
 P (916) 575-7170 F (916) 575-7292 www.optometry .ca.gov



Continuing Education Course
 Approval Checklist

Title:

Provider Name:

Completed Application

Open to all Optometrists? Yes No

Maintain Record Agreement? Yes No

Correct Application Fee

Detailed Course Summary

Detailed Course Outline

PowerPoint and/or other Presentation Materials **Images are not showing**

Advertising (optional)

CV for EACH Course Instructor

License Verification for Each Course Instructor

Disciplinary History? Yes No



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CONTINUING EDUCATION COURSE APPROVAL APPLICATION

\$50 Mandatory Fee

\$50 Paid

Pursuant to California Code of Regulations (CCR) § 1536, the Board will approve continuing education (CE) courses after receiving the applicable fee, the requested information below and it has been determined that the course meets criteria specified in CCR § 1536(g).

In addition to the information requested below, please attach a copy of the course schedule, a detailed course outline and presentation materials (e.g., PowerPoint presentation). Applications must be submitted 45 days prior to the course presentation date.

Please type or print clearly.

Course Title Review of Uveitis	Course Presentation Date 05 / 18 / 2017
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Course Provider Contact Information

Provider Name Craig Leong J. (First) (Last) (Middle)	
Provider Mailing Address Street 122 La Casa Via, #223 City Walnut Creek State CA Zip 94598	
Provider Email Address cleong@bayarearetina.com	
Will the proposed course be open to all California licensed optometrists?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Do you agree to maintain and furnish to the Board and/or attending licensee such records of course content and attendance as the Board requires, for a period of at least three years from the date of course presentation?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

Course Instructor Information

Please provide the information below and attach the curriculum vitae for each instructor or lecturer involved in the course. If there are more instructors in the course, please provide the requested information on a separate sheet of paper.

Instructor Name Craig Leong Jan (First) (Last) (Middle)	
License Number G28041	License Type M.D.
Phone Number (925) 943-6800	Email Address cleong@bayarearetina.com

I declare under penalty of perjury under the laws of the State of California that all the information submitted on this form and on any accompanying attachments submitted is true and correct.

[Signature]
 Signature of Course Provider

4/17/17
 Date

Attention Board of Optometry.

To whom it might concern,

Along with this letter you will find CV's from all three doctors, CE applications, Summaries, Outlines, and Presentation materials. I apologized for the information being a little late but one of the doctors was Out of town and I didn't get his presentation information until much later.

Let me know if you need any other information.

Hedy Rodriguez

Batra Vision Medical Group

hedyr@batravisision.com

Uveitis

Uveitis is an autoimmune disease of the eye that refers to a number of intraocular inflammatory conditions. Uveitis can be associated with various systemic diseases and it is important for an eye care provider to recognize the possible ocular manifestations of these systemic conditions

Examples of common anterior, intermediate and posterior uveitis will be presented. Panuveitis as well and the ocular complications of HIV will also be discussed. The etiology, clinical findings, diagnostic testing and treatment of each disease entity will be summarized.

Following this lecture, attendees should be able to recognize the findings, categorize the types and understand how the most common causes of uveitis are currently managed.

Definition of Uveitis

Overview

Classification of Uveitis

Granulomatous vs Non-granulomatous

Unilateral vs Bilateral

Symptoms

Ocular findings

Standardized Grading Scale for Anterior Chamber Inflammation

Examples of Anterior Uveitis

- Traumatic iritis
- HLA-B27
- Herpes simplex uveitis
- Juvenile Idiopathic Arthritis

Examples of Intermediate Uveitis

- Pars Planitis
- Multiple Sclerosis
- Endophthalmitis

Examples of Posterior Uveitis

- Toxoplasmosis

Examples of Panuveitis

- Sarcoidosis
- Syphilis
- Tuberculosis
- Vogt-Koyanagi-Harada Disease

Ocular Complications of HIV

- HIV Retinopathy
- Panuveitis secondary to syphilis and toxoplasmosis
- Ocular lymphoma
- Fungal Endophthalmitis
- Frosted Branch Angiitis
- Cytomegalovirus (CMV) Retinitis

Herpes Retinitis

- Acute Retinal Necrosis (ARN)
- Progressive Outer Retinal Necrosis (PORN)

1 2  **Uveitis: Inflammation of the Uvea**3  **Overview**

- 58/100,000 persons
- Whites > non-whites
- Genders equally affected (but women outlive men)
- Increasing prevalence with age
- Third leading cause of blindness in the developed countries
- 39% of chronic anterior uveitis is truly idiopathic

4  **Classification of Uveitis**

Anterior Uveitis

- Iritis: Inflammation of the iris
- Iridocyclitis: Inflammation of the iris and ciliary body

5  **Classification of Uveitis**

Intermediate Uveitis / Pars Planitis

- Pars Plana: "Snowbank" inflammatory exudates
- Vitreous: inflammatory cells and clumped WBC's in the vitreous

6  **Classification of Uveitis**

Posterior Uveitis

- Choroiditis: Inflammation primarily in the choroid, e.g., Punctate Inner Choroiditis (PIC)

7  **Classification of Uveitis**

Posterior Uveitis

- Chorioretinitis: Inflammation of the choroid > retina, e.g., Presumed Ocular Histoplasmosis Syndrome (POHS)

8  **Classification of Uveitis**

Posterior Uveitis

- Retinochoroiditis: Inflammation in the retina > choroid, e.g., Toxoplasmosis retinochoroiditis

9  **Classification of Uveitis**

Panuveitis

- Inflammation of all of the layers of the uvea, e.g., uveitis secondary to tuberculosis, syphilis, sarcoidosis, Vogt Koyanagi Harada Disease, sympathetic ophthalmia

10  **Classification of Uveitis**

Non-granulomatous

- Fine deposits of lymphocytes on corneal endothelium
- Etiology: Uveitis secondary to HLA-B27, juvenile idiopathic arthritis, multiple sclerosis, inflammatory bowel disease, psoriasis, systemic lupus erythematosus

11  **Classification of Uveitis**

Granulomatous

- Thick deposits of lymphocytes and epithelioid cells on corneal endothelium
- Etiology: Uveitis secondary to syphilis, sarcoidosis, tuberculosis, toxoplasmosis, Vogt Koyanagi Harada Disease, herpes zoster/simplex, sympathetic ophthalmia

- 12 **Unilateral vs. Bilateral**
Unilateral
- Etiology: Infectious, traumatic, post-operative, idiopathic
- 13 **Unilateral vs. Bilateral**
Bilateral
- Etiology: Systemic infection, autoimmune, granulomatous disease
- 14 **Uveitis Symptoms**
- Blurred vision and ocular pain
 - Ocular redness / circumlimbal flush
 - Light sensitivity / photophobia
- 15 **Ocular Findings**
- Inflammatory cells and flare (protein) in the aqueous
 - Keratic precipitates on corneal endothelium
 -
- 16 **Ocular Findings**
- Posterior synechiae (pupillary adhesions to lens)
 - Iris atrophy (secondary to chronic iritis)
 - Iris nodules (WBC's on anterior iris stroma)
- 17 **Ocular Findings**
- Hypopyon (layered WBC's in inferior AC angle)
 - Inflammatory glaucoma (inflammatory blockage of trabecular meshwork)
 - Inflammatory hypotony (ciliary body shutdown)
- 18 **Ocular Findings**
- Cataract (due to inflammation or steroid treatment)
 - Vitritis: Vitreous inflammation
 - Pars plana "snowbank" inflammatory exudates
- 19 **Ocular Findings**
- Chorioretinal inflammation
 - Retinal vasculitis
- 20 **Ocular Findings**
- Optic disc hyperemia
 - Cystoid macular edema
 -
- 21 **Standardized Grading Scale for Anterior Chamber Inflammation**
- 22 **Anterior Uveitis: Traumatic Iritis**
- Etiology: accidental blunt trauma, fist fights, sports injuries, car accidents
 - 20% of iritis
 - Findings: cells and flare, hyphema, subconjunctival hemorrhage
 - Management: cycloplegic and steroid eyedrops
- 23 **Anterior Uveitis: Human Leukocyte Antigen HLA-B27 Uveitis**

- Associated diseases: Ankylosing spondylitis, reactive arthritis (Reiter syndrome), inflammatory bowel disease, psoriatic arthritis
 - Incidence: 40-70% of acute anterior uveitis
 - Findings: AC fibrin, hypopyon, posterior synechiae
- 24 **Anterior Uveitis: Human Leukocyte Antigen HLA-B27 Uveitis**
- Diagnosis: HLA-B27 blood test
 - Management: Topical steroid and cycloplegic eyedrops, periocular/intravitreal steroid injections, NSAIDs, systemic steroids, cyclosporine, methotrexate, azathioprine, etanercept (Enbrel)
- 25 **Anterior Uveitis: Herpes Simplex Keratouveitis**
- Etiology: Herpes simplex virus
 - Incidence: 9% of anterior uveitis
 - Findings: 85% anterior > 15% posterior uveitis, decreased corneal sensitivity, iris atrophy, keratic precipitates, posterior synechiae, glaucoma
- 26 **Anterior Uveitis: Herpes Simplex Keratouveitis**
- Clinical diagnosis: unilateral anterior uveitis with high IOP
 - Laboratory diagnosis: Negative HSV titer rules out HSV; PCR testing for HSV DNA in the aqueous
 - Management: cycloplegic and steroid eyedrops, treat glaucoma, oral antiviral medications (Acyclovir, valacyclovir, famciclovir)
- 27 **Anterior Uveitis: Juvenile Idiopathic Arthritis**
- Etiology: probable autoimmune reaction to ocular antigens with a possible genetic predisposition
 - Incidence: 6% of uveitis are in children of which the most frequent cause is JIA. 10-20% of JIA patient will develop uveitis
 - Findings: AC cells with white eye, keratic precipitates, posterior synechiae, band keratopathy, cataract, CME
- 28 **Anterior Uveitis: Juvenile Idiopathic Arthritis**
- Diagnosis: ANA is positive in 80%, HLA-DR5
 - Management: Steroid and cycloplegic eyedrops, NSAIDs, systemic steroids, methotrexate, etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), abatacept (Orencia), tocilizumab (Actemra)
- 29 **Intermediate Uveitis: Pars planitis**
- Etiology: Autoimmune
 - Incidence: 10% of uveitis is due to pars planitis
 - Findings: Vitreous cells, pars plana "snowbank" exudates, retinal vasculitis, CME, cataract, inflammatory glaucoma
- 30 **Intermediate Uveitis: Pars planitis**
- Diagnosis: Clinical presentation; no specific testing available
 - Management: Periocular steroid injections, cryopexy of pars plana, vitrectomy+endolaser, treatment of inflammatory glaucoma, cyclosporine, azathioprine, methotrexate, cyclophosphamide
- 31 **Intermediate Uveitis: Multiple Sclerosis**
- Etiology: Multiple sclerosis

- Incidence: 14% of uveitis patients have MS, 27% of MS patients have uveitis
 - Findings: Retinal vasculitis, CME, vitreous cells, retrobulbar neuritis
- 32 **Intermediate Uveitis: Multiple Sclerosis**
- Diagnosis: HLA-DR2 antigen, brain MRI scan
 - Management: Periocular steroid injections, treatment of inflammatory glaucoma, cyclosporine, azathioprine, methotrexate, cyclophosphamide
- 33 **Intermediate Uveitis: Post-operative Endophthalmitis**
- Presentation: 3-14 days post-op, progressively worsens
 - Symptoms: Blurred vision, redness, pain
 - Incidence: 0.08-0.68% after cataract surgery, 0.2-0.4% after secondary IOL, 0.2-9.6% after glaucoma filter, 0.03-0.05% after vitrectomy
- 34 **Intermediate Uveitis: Post-operative Endophthalmitis**
- Findings: corneal edema, AC cells and fibrin, hypopyon, vitritis, retinal vasculitis and infectious retinitis
 - Management: Sample the aqueous / vitreous for culture+sensitivity of organisms, intravitreal injection of vancomycin and ceftazidime, vitrectomy with intravitreal antibiotics if Va is only LP
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 -
 -
- 35 **Intermediate Uveitis: Endogenous Endophthalmitis**
- Endogenous: infection that spreads from body to eye
 - Associated conditions: diabetes, HIV, IV drug abuse, immunosuppressive therapy, indwelling catheter, recent intravenous infusion
 - Incidence: 2-8% of endophthalmitis cases
- 36 **Intermediate Uveitis: Endogenous Endophthalmitis**
- Findings: Infectious retinitis, vitritis
 - Diagnosis: Culture blood, vitreous and any indwelling catheter for bacteria and fungus
 - Management: Initiate treatment with intravenous vancomycin and ceftazidime, revise antibiotics depending upon culture results
- 37 **Posterior Uveitis: Toxoplasmosis**
- Etiology: Toxoplasma gondii, a parasite carried by cats. Intermediate hosts are humans, mammals, birds and reptiles. Most common cause of infectious posterior uveitis
- 38 **Posterior Uveitis: Toxoplasmosis**
- Congenital: passed from mother to fetus in utero with later reactivation of scar
 - Acquired: primarily in immunocompromised patients
 - Ocular findings: Active retinochoroiditis and vitritis adjacent to a congenital scar; large, confluent and bilateral lesions in immunocompromised patients.
 -
- 39 **Posterior Uveitis: Toxoplasmosis**
- Diagnosis: Toxoplasma IgM and IgG titers, PCR of aqueous and vitreous
 - Treatment: Pyrimethamine, sulfadiazine and oral steroids. Alternative treatment regimens include systemic / intravitreal clindamycin, oral Bactrim, azithromycin, atovaquone, intravitreal dexamethasone

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40 **Panuveitis: Sarcoidosis**

- Etiology: Unknown. Possible genetic and environmental factors. Possible association with HLA-DRB1 antigen and exposure to tuberculosis.
 - Incidence: 3-10% of all uveitis. African Americans > whites, females>males
 - Symptoms: blurred vision, redness, floaters, eye pain
-

41 **Panuveitis: Sarcoidosis**

- Ocular findings: conjunctival, scleral and lacrimal gland granulomas, granulomatous anterior uveitis, iris nodules, posterior synechiae, cataract, vitritis, choroiditis, retinal vasculitis (candle-wax drippings), CME, optic neuropathy and inflammatory glaucoma
-

42 **Panuveitis: Sarcoidosis**

- Systemic findings: non-caseating granulomas, pulmonary hilar adenopathy, erythema nodosum, lymphadenopathy, arthritis, cough and polymyositis
 - Diagnosis: serum angiotensin converting enzyme (ACE) and serum lysozyme, chest X-ray, chest CT scan, conjunctival biopsy, whole body gallium scan
-

43 **Panuveitis: Sarcoidosis**

- Treatment: Topical steroid and cycloplegic eyedrops, oral steroids, periocular steroid injections, methotrexate, cyclosporine, infliximab (Remicade)
-
-

44 **Panuveitis: Syphilis**

- Etiology: STD infection by Treponema Pallidum; Acquired >>Congenital cases
- Incidence; <5% of all uveitis cases; high risk sex is the key factor; 67% of acquired cases occur in men who have sex with men; high rate of HIV coinfection

45 **Panuveitis: Syphilis**

- Ocular findings: Iridocyclitis, iris nodules, keratic precipitates, vitritis, multifocal chorioretinitis, retinal vasculitis, CME, optic neuropathy, Argyll Robertson pupil, inflammatory glaucoma
 - Systemic findings: Genital chancres, skin rash, impaired balance, deafness, dementia, aortic aneurysm
-
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46 **Panuveitis: Syphilis**

- Diagnosis: RPR (Nonspecific) and FTA-ABS (specific), lumbar puncture for CSF cells, protein and VDRL serology
 - Treatment: Topical steroid and cycloplegic eyedrops
 - Neurosyphilis: Intravenous Penicillin G x 14 days
-

47 **Panuveitis: Tuberculosis**

- Etiology: Mycobacterium tuberculosis, an airborne pathogen with primary pulmonary involvement

- Ocular findings: granulomatous panuveitis, vitritis, choroiditis, vasculitis, CME and optic neuropathy
- Systemic findings: Secondary involvement of the bones, brain, liver, kidneys and heart
-

48 **Panuveitis: Tuberculosis**

- Incidence: 3 cases/100,000 people in USA; 1-2% of all cases of uveitis; higher risk in immunocompromised patients, health care workers and immigrants from endemic countries
- Diagnosis: PPD skin test, quantiferon gold blood test, chest x-ray, sputum culture, PCR of aqueous/vitreous

49 **Panuveitis: Tuberculosis**

Treatment:

- Systemic tuberculosis is treated with rifampin, isoniazid, ethambutol, and pyrazinamide
- Ocular manifestations are treated with topical steroid and cycloplegic eyedrops in conjunction with systemic antibiotics

50 **Panuveitis: Vogt Koyanagi Harada Disease**

- Etiology: Unknown but assumed to be autoimmune
- Incidence: 1-3% of uveitis in USA; 7-9% of uveitis in Japan; darker pigmented individuals; women>men
- Symptoms: Headache, photophobia, blurred vision, nausea, eye pain

51 **Panuveitis: Vogt Koyanagi Harada Disease**

- Ocular Findings: Choroiditis with multifocal serous retinal detachments, optic disc hyperemia, granulomatous panuveitis, choroidal depigmentation
- Systemic Findings: Poliosis (loss of melanin in hair), vitiligo (loss of melanin in skin), alopecia (loss of hair), tinnitus (ringing in ears), dysacusis (loss of hearing)

52 **Panuveitis: Vogt Koyanagi Harada Disease**

- Diagnosis: Fluorescein and ICG angiography, OCT scan, fundus hyperautofluorescence; lumbar puncture shows CSF pleocytosis (increased WBC's and protein)
- Treatment: Systemic corticosteroids, methotrexate, azathioprine, cyclosporine

53 **Ocular Complications of HIV**

- Etiology: HIV incidence (37,600 new cases/year in 2014) declining due to HAART (highly active anti-retroviral therapy. Ocular complications occur in 70-80% HIV patients; increased risk when CD4 count drops to < 200 cells/cubic mm
- Ocular Findings: Kaposi's sarcoma, molluscum contagiosum

54 **Ocular Complications of HIV**

- Ocular Findings: Herpes zoster ophthalmicus, herpes keratitis
-

55 **Ocular Complications of HIV**

- Ocular Findings: HIV retinopathy, ocular syphilis, toxoplasmosis retinochoroiditis, ocular lymphoma,

56 **Ocular Complications of HIV**

- Ocular Findings: fungal endophthalmitis

57 **Ocular Complications of HIV**

- Ocular Findings: Frosted branch angiitis, cytomegalovirus (CMV) retinitis

58 **Panuveitis: ARN vs. PORN**

- ARN: Acute Retinal Necrosis (not immunocompromised)
- PORN: Progressive Outer Retinal Necrosis (immunocompromised or HIV)
- Etiology: Herpes (zoster or simplex) retinitis in both conditions

59 **Panuveitis: ARN vs. PORN**

- Symptoms: Blurred vision, vitreous floaters, photophobia initially in one eye
- Ocular Findings: Rapidly progressive peripheral retinal necrosis with severe panuveitis and occlusive retinal vasculitis, retinal detachment, optic atrophy
- Diagnosis: PCR of intraocular fluids for herpes DNA

60 **Panuveitis: ARN vs. PORN**

- Medical therapy: Intravenous acyclovir x 14 days followed by oral valacyclovir x 3 months or longer
- Surgical Therapy: Prophylactic laser photocoagulation of large retinal breaks if retina not detached. Vitrectomy with endolaser and silicone oil tamponade if retina is detached.

61 **Panuveitis: ARN vs. PORN**

- Medical therapy: Intravenous acyclovir x 14 days followed by oral valacyclovir x 3 months or longer
- Surgical Therapy: Prophylactic laser photocoagulation of large retinal breaks if retina not detached. Vitrectomy with endolaser and silicone oil tamponade if retina is detached.

62 **The Final Word**

- History, history, history: Most cases of uveitis have a cause and the patient's medical history will give you the clues to finding it.
- Always dilate and examine both eyes: Anterior segment inflammation often has a posterior component that will indicate the cause.
- Be wary of simply treating with topical steroids without determining the cause of the uveitis: steroids suppress inflammation, delay making a diagnosis and, in some cases, can allow the underlying condition to worsen.

Born: Dinuba, California, USA 4/19/47

College: Stanford University, Palo Alto, CA B.A. in Psychology 1965 - 1969

Medical School: Northwestern University, Chicago, IL 1969 - 1973

Internship: Beth Israel Medical Center, New York, NY 7/1973 - 6/1974

Residency: Ophthalmology, State University of New York, Downstate Medical Center, Brooklyn, NY 7/1974 - 6/1977

Fellowship: Retina-Vitreous Fellowship

Manhattan Eye, Ear and Throat Hospital
Cornell University Medical Center
New York, NY 7/1977 - 6/1978

Board Certified: American Board of Ophthalmology 1979

Medical Licensure: New York, U.S. – 8/1972 California, U.S. – 6/1975

Private Practice: Bay Area Retina Associates, California 1979 - Present

Assistant Clinical Professor of Ophthalmology

University of California San Francisco Medical Center
San Francisco, CA 1980 - present

Clinical Trials

Principal Investigator – VAM Study, Verteporfin and Age Related Macular Degeneration 1999 – 2000.
Sponsor – Novartis, Inc.

Principal Investigator – FOCUS Study for RhuFab V2 Phase II – 2002
Sponsor – Genentech, Inc.

Principal Investigator – MARINA Study for RhuFab V2 Phase III -2003
Sponsor – Genentech, Inc.

Principal Investigator – Ruboxistarin Study for Diabetic Macular Edema Phase III -2004 Sponsor –Eli Lilly, Inc.

Investigator – SCORE Study for BRVO/CRVO – 2004
Sponsor – NIH/NEI

Investigator – DRCR Studies for Diabetic Retinopathy – 2004
Sponsor – NIH/NEI

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FAX (510) 317-1113

5980 STONERIDGE DRIVE
SUITE 117
PLEASANTON, CA 94588
(925) 463-8200
FAX: (925) 463-8201

Principal Investigator – HORIZON Study for RhuFab V2 Phase IIIb -2005
Sponsor – Genentech, Inc.

Principal Investigator – SAILOR Study for RhuFab V2 Phase IIIb -2005
Sponsor – Genentech, Inc.

Principal Investigator – ACU201-Cand5 Study Phase II -2005
Sponsor – Acuity Pharmaceuticals, Inc.

Investigator – PDEX Study-Combination Triple Therapy vs. Lucentis Monotherapy – 2006
Sponsor – Bay Area Retina Associates IST

Investigator – BRAVO Study for RhuFab V2 Phase III -2007
Sponsor – Genentech, Inc.

Investigator – CRUISE Study for RhuFab V2 Phase III -2007
Sponsor – Genentech, Inc.

Investigator – QUARK 003 Study for REDD14 siRNA Phase I -2007
Sponsor – Quark Pharmaceuticals, Inc.

Investigator – LUCEDEX Lucentis and Dexamethasone vs. Monotherapy Lucentis – 2008
Sponsor- Bay Area Retina Associates

Investigator- OASIS - Ocriplasmin for Treatment for Symptomatic Vitreomacular Adhesion Including Macular Hole- 2011
Sponsor-ThromboGenics

Investigator- SPECTRI - Lampalizumab Intravitreal Injections in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration- 2014
Sponsor-Hoffmann-La Roche

Investigator- STOMP - Short-Term Oral Mifepristone for Central Serous Choroidopathy. A Placebo-controlled Dose Ranging Study of Mifepristone in the Treatment of CSC, IST- 2015
Sponsor: Roger Goldberg, M.D.

Investigator- VAPOR 1–DE-120 Injectable Solution for Age-related Macular Degeneration- 2015
Sponsor: Santen, Inc.

Investigator- AVENUE - RG7716 Administered Intravitreally in Patients with Choroidal Neovascularization Secondary to Age-Related Macular Degeneration- 2015
Sponsor: Hoffmann-La Roche

Investigator- BOULEVARD - RO6867461 in Participants with Center-Involving Diabetic Macular Edema (CI-DME) Phase II - 2016
Sponsor: Hoffmann-La Roche

Principal Investigator- PAVE - DE-122 Injectable Solution for the Treatment of Refractory Exudative Age-related Macular Degeneration Phase I/II- 2015
Sponsor: Santen, Inc.

Investigator- OMASPECT - Lampalizumab in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration Who Have Completed a Roche-Sponsored Study – 2016
Sponsor: Hoffmann-La Roche, 2016

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Examples of Intermediate Uveitis

- Pars Planitis
- Multiple Sclerosis
- Endophthalmitis

Examples of Posterior Uveitis

- Toxoplasmosis

Examples of Panuveitis

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- Syphilis
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Herpes Retinitis

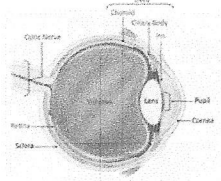
- Acute Retinal Necrosis (ARN)
- Progressive Outer Retinal Necrosis (PORN)

Uveitis



Craig J. Leong, M.D.
Bay Area Retina Associates
May 18, 2017

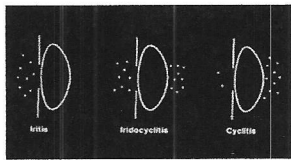
Uveitis: Inflammation of the Uvea



Overview

- 58/100,000 persons
- Whites > non-whites
- Genders equally affected (but women outlive men)
- Increasing prevalence with age
- Third leading cause of blindness in the developed countries
- 39% of chronic anterior uveitis is truly idiopathic

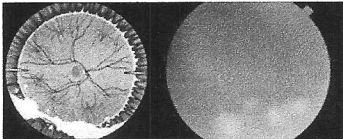
Classification of Uveitis



Anterior Uveitis

- Iritis: Inflammation of the iris
- Iridocyclitis: Inflammation of the iris and ciliary body

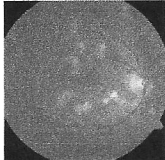
Classification of Uveitis



Intermediate Uveitis / Pars Planitis

- Pars Plana: "Snowbank" inflammatory exudates
- Vitreous: inflammatory cells and clumped WBC's in the vitreous

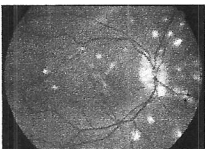
Classification of Uveitis



Posterior Uveitis

- Choroiditis: Inflammation primarily in the choroid, e.g., Punctate Inner Choroiditis (PIC)

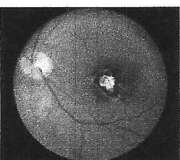
Classification of Uveitis



Posterior Uveitis

- Chorioretinitis: Inflammation of the choroid > retina, e.g., Presumed Ocular Histoplasmosis Syndrome (POHS)

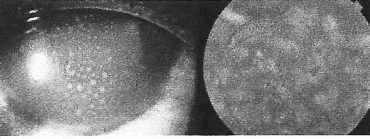
Classification of Uveitis



Posterior Uveitis

- Retinochoroiditis: Inflammation in the retina > choroid, e.g., Toxoplasmosis retinochoroiditis

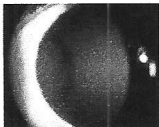
Classification of Uveitis



Panuveitis

- Inflammation of all of the layers of the uvea, e.g., uveitis secondary to tuberculosis, syphilis, sarcoidosis, Vogt Koyanagi Harada Disease, sympathetic ophthalmia


Classification of Uveitis



Non-granulomatous

- Fine deposits of lymphocytes on corneal endothelium
- Etiology: Uveitis secondary to HLA-B27, juvenile idiopathic arthritis, multiple sclerosis, inflammatory bowel disease, psoriasis, systemic lupus erythematosus


Classification of Uveitis



Granulomatous

- Thick deposits of lymphocytes and epithelioid cells on corneal endothelium
- Etiology: Uveitis secondary to syphilis, sarcoidosis, tuberculosis, toxoplasmosis, Vogt Koyanagi Harada Disease, herpes zoster/simplex, sympathetic ophthalmia


Unilateral vs. Bilateral



Unilateral

- Etiology: Infectious, traumatic, post-operative, idiopathic

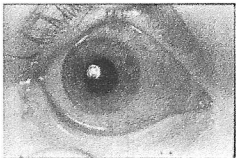
Unilateral vs. Bilateral



Bilateral

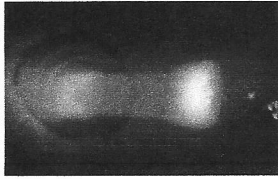
- Etiology: Systemic infection, autoimmune, granulomatous disease

Uveitis Symptoms



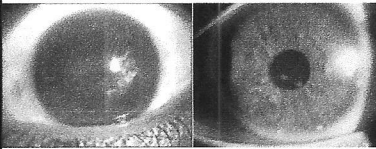
- Blurred vision and ocular pain
- Ocular redness / circumlimbal flush
- Light sensitivity / photophobia

Ocular Findings




- Inflammatory cells and flare (protein) in the aqueous
- Keratic precipitates on corneal endothelium

Ocular Findings



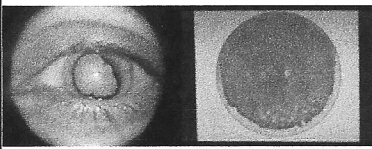
- Posterior synechiae (pupillary adhesions to lens)
- Iris atrophy (secondary to chronic iritis)
- Iris nodules (WBC's on anterior iris stroma)

Ocular Findings



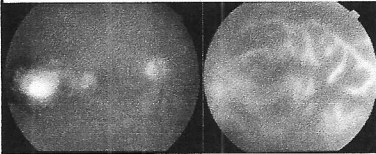
- Hypopyon (layered WBC's in inferior AC angle)
- Inflammatory glaucoma (inflammatory blockage of trabecular meshwork)
- Inflammatory hypotony (ciliary body shutdown)

Ocular Findings



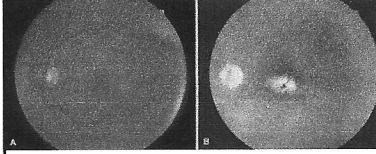
- Cataract (due to inflammation or steroid treatment)
- Vitritis: Vitreous inflammation
- Pars plana "snowbank" inflammatory exudates

Ocular Findings



- Chorioretinal inflammation
- Retinal vasculitis

Ocular Findings



- Optic disc hyperemia
- Cystoid macular edema


Standardized Grading Scale for Anterior Chamber Inflammation

Standardized Grading Scales for Uveitis*	
SIS Grading Scheme for Anterior Chamber Cells	
Grade	Cells in Field
0	= 0
1.0+	1-5
1+	6-15
2+	16-25
3+	26-50
4+	50+

*Adapted from the ISUVEIS


SIS Grading Scheme for Anterior Chamber Flare	
Grade	Description
0	None
1+	Faint
2+	Markedly increased opacity
3+	Marked (obscure corneal haze)
4+	Intense (obscure cornea)

Anterior Uveitis: Traumatic Iritis




- Etiology: accidental blunt trauma, fist fights, sports injuries, car accidents
- 20% of iritis
- Findings: cells and flare, hyphema, subconjunctival hemorrhage
- Management: cycloplegic and steroid eyedrops

Anterior Uveitis: Human Leukocyte Antigen HLA-B27 Uveitis




- Associated diseases: Ankylosing spondylitis, reactive arthritis (Reiter syndrome), inflammatory bowel disease, psoriatic arthritis
- Incidence: 40-70% of acute anterior uveitis
- Findings: AC fibrin, hypopyon, posterior synechiae

Anterior Uveitis: Human Leukocyte Antigen HLA-B27 Uveitis



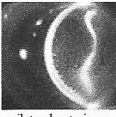
- Diagnosis: HLA-B27 blood test
- Management: Topical steroid and cycloplegic eyedrops, periocular/intravitreal steroid injections, NSAIDs, systemic steroids, cyclosporine, methotrexate, azathioprine, etanercept (Enbrel)

Anterior Uveitis: Herpes Simplex Keratouveitis



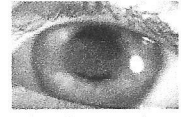
- Etiology: Herpes simplex virus
- Incidence: 9% of anterior uveitis
- Findings: 85% anterior > 15% posterior uveitis, decreased corneal sensitivity, iris atrophy, keratic precipitates, posterior synechiae, glaucoma

Anterior Uveitis: Herpes Simplex Keratouveitis



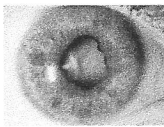
- Clinical diagnosis: unilateral anterior uveitis with high IOP
- Laboratory diagnosis: Negative HSV titer rules out HSV; PCR testing for HSV DNA in the aqueous
- Management: cycloplegic and steroid eyedrops, treat glaucoma, oral antiviral medications (Acyclovir, valacyclovir, famciclovir)

Anterior Uveitis: Juvenile Idiopathic Arthritis



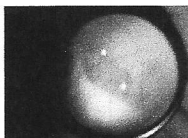
- Etiology: probable autoimmune reaction to ocular antigens with a possible genetic predisposition
- Incidence: 6% of uveitis are in children of which the most frequent cause is JIA. 10-20% of JIA patient will develop uveitis
- Findings: AC cells with white eye, keratic precipitates, posterior synechiae, band keratopathy, cataract, CME

Anterior Uveitis: Juvenile Idiopathic Arthritis



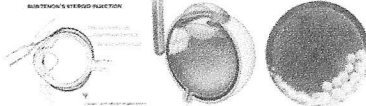
- Diagnosis: ANA is positive in 80%, HLA-DR5
- Management: Steroid and cycloplegic eyedrops, NSAIDs, systemic steroids, methotrexate, etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), abatacept (Orencia), tocilizumab (Actemra)

Intermediate Uveitis: Pars planitis



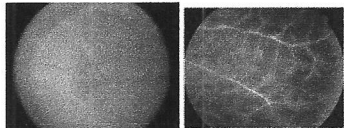
- Etiology: Autoimmune
- Incidence: 10% of uveitis is due to pars planitis
- Findings: Vitreous cells, pars plana "snowbank" exudates, retinal vasculitis, CME, cataract, inflammatory glaucoma

Intermediate Uveitis: Pars planitis



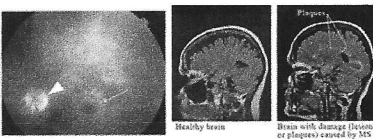
- Diagnosis: Clinical presentation; no specific testing available
- Management: Periocular steroid injections, cryopexy of pars plana, vitrectomy+endolaser, treatment of inflammatory glaucoma, cyclosporine, azathioprine, methotrexate, cyclophosphamide

Intermediate Uveitis: Multiple Sclerosis




- Etiology: Multiple sclerosis
- Incidence: 14% of uveitis patients have MS, 27% of MS patients have uveitis
- Findings: Retinal vasculitis, CME, vitreous cells, retrolubar neuritis

Intermediate Uveitis: Multiple Sclerosis



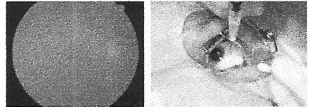
- Diagnosis: HLA-DR2 antigen, brain MRI scan
- Management: Periocular steroid injections, treatment of inflammatory glaucoma, cyclosporine, azathioprine, methotrexate, cyclophosphamide

Intermediate Uveitis: Post-operative Endophthalmitis



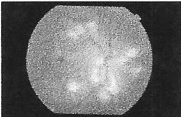
- Presentation: 3-14 days post-op, progressively worsens
- Symptoms: Blurred vision, redness, pain
- Incidence: 0.08-0.68% after cataract surgery, 0.2-0.4% after secondary IOL, 0.2-9.6% after glaucoma filter, 0.03-0.05% after vitrectomy

Intermediate Uveitis: Post-operative Endophthalmitis



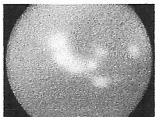
- Findings: corneal edema, AC cells and fibrin, hypopyon, vitritis, retinal vasculitis and infectious retinitis
- Management: Sample the aqueous / vitreous for culture+sensitivity of organisms, intravitreal injection of vancomycin and ceftazidime, vitrectomy with intravitreal antibiotics if Va is only LP

Intermediate Uveitis: Endogenous Endophthalmitis



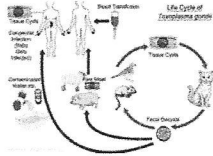
- Endogenous: infection that spreads from body to eye
- Associated conditions: diabetes, HIV, IV drug abuse, immunosuppressive therapy, indwelling catheter, recent intravenous infusion
- Incidence: 2-8% of endophthalmitis cases

Intermediate Uveitis: Endogenous Endophthalmitis



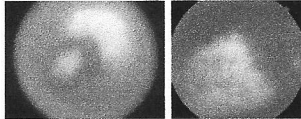
- Findings: Infectious retinitis, vitritis
- Diagnosis: Culture blood, vitreous and any indwelling catheter for bacteria and fungus
- Management: Initiate treatment with intravenous vancomycin and ceftazidime, revise antibiotics depending upon culture results

Posterior Uveitis: Toxoplasmosis



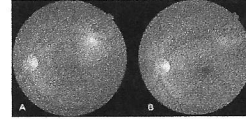
- Etiology: Toxoplasma gondii, a parasite carried by cats. Intermediate hosts are humans, mammals, birds and reptiles. Most common cause of infectious posterior uveitis

Posterior Uveitis: Toxoplasmosis



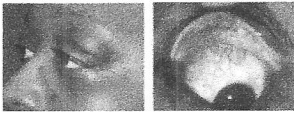
- Congenital: passed from mother to fetus in utero with later reactivation of scar
- Acquired: primarily in immunocompromised patients
- Ocular findings: Active retinochoroiditis and vitritis adjacent to a congenital scar, large, confluent and bilateral lesions in immunocompromised patients

Posterior Uveitis: Toxoplasmosis



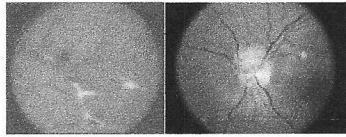
- Diagnosis: Toxoplasma IgM and IgG titers, PCR of aqueous and vitreous
- Treatment: Pyrimethamine, sulfadiazine and oral steroids. Alternative treatment regimens include systemic / intravitreal clindamycin, oral Bactrim, azithromycin, atovaquone, intravitreal dexamethasone

Panuveitis: Sarcoidosis



- Etiology: Unknown. Possible genetic and environmental factors. Possible association with HLA-DRB1 antigen and exposure to tuberculosis.
- Incidence: 3-10% of all uveitis. African Americans > whites, females>males
- Symptoms: blurred vision, redness, floaters, eye pain

Panuveitis: Sarcoidosis



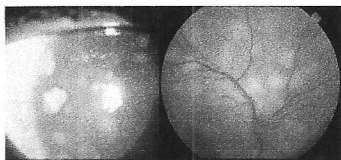
- Ocular findings: conjunctival, scleral and lacrimal gland granulomas, granulomatous anterior uveitis, iris nodules, posterior synechiae, cataract, vitritis, choroiditis, retinal vasculitis (candle-wax drippings), CME, optic neuropathy and inflammatory glaucoma

Panuveitis: Sarcoidosis



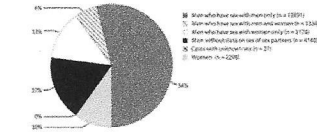
- Systemic findings: non-caseating granulomas, pulmonary hilar adenopathy, erythema nodosum, lymphadenopathy, arthritis, cough and polymyositis
- Diagnosis: serum angiotensin converting enzyme (ACE) and serum lysozyme, chest X-ray, chest CT scan, conjunctival biopsy, whole body gallium scan

Panuveitis: Sarcoidosis



- Treatment: Topical steroid and cycloplegic eyedrops, oral steroids, periocular steroid injections, methotrexate, cyclosporine, infliximab (Remicade)

Panuveitis: Syphilis



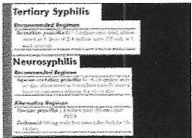
- Etiology: STD infection by Treponema Pallidum; Acquired >> Congenital cases
- Incidence; <5% of all uveitis cases, high risk sex is the key factor; 67% of acquired cases occur in men who have sex with men; high rate of HIV coinfection

Panuveitis: Syphilis



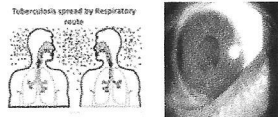
- Ocular findings: Iridocyclitis, iris nodules, keratic precipitates, vitritis, multifocal chorioretinitis, retinal vasculitis, CME, optic neuropathy, Argyll Robertson pupil, inflammatory glaucoma
- Systemic findings: Genital chancres, skin rash, impaired balance, deafness, dementia, aortic aneurysm

Panuveitis: Syphilis



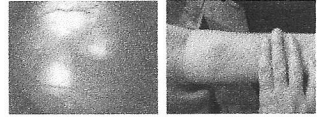
- Diagnosis: RPR (Nonspecific) and FTA-ABS (specific), lumbar puncture for CSF cells, protein and VDRL serology
- Treatment: Topical steroid and cycloplegic eyedrops
- Neurosyphilis: Intravenous Penicillin G x 14 days

Panuveitis: Tuberculosis



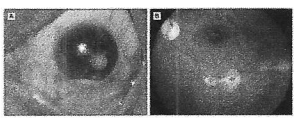
- Etiology: Mycobacterium tuberculosis, an airborne pathogen with primary pulmonary involvement
- Ocular findings: granulomatous panuveitis, vitritis, choroiditis, vasculitis, CME and optic neuropathy
- Systemic findings: Secondary involvement of the bones, brain, liver, kidneys and heart

Panuveitis: Tuberculosis



- Incidence: 3 cases/100,000 people in USA; 1-2% of all cases of uveitis; higher risk in immunocompromised patients, health care workers and immigrants from endemic countries
- Diagnosis: PPD skin test, quantiferon gold blood test, chest x-ray, sputum culture, PCR of aqueous/vitreous


Panuveitis: Tuberculosis



Treatment:

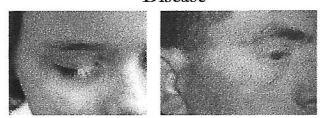
- Systemic tuberculosis is treated with rifampin, isoniazid, ethambutol, and pyrazinamide
- Ocular manifestations are treated with topical steroid and cycloplegic eyedrops in conjunction with systemic antibiotics

Panuveitis: Vogt Koyanagi Harada Disease



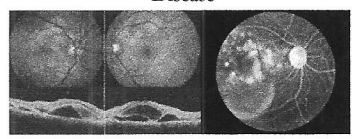
- Etiology: Unknown but assumed to be autoimmune
- Incidence: 1-3% of uveitis in USA; 7-9% of uveitis in Japan; darker pigmented individuals; women>men
- Symptoms: Headache, photophobia, blurred vision, nausea, eye pain

Panuveitis: Vogt Koyanagi Harada Disease



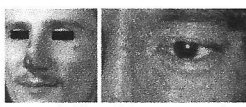
- Ocular Findings: Choroiditis with multifocal serous retinal detachments, optic disc hyperemia, granulomatous panuveitis, choroidal depigmentation
- Systemic Findings: Poliosis (loss of melanin in hair), vitiligo (loss of melanin in skin), alopecia (loss of hair), tinnitus (ringing in ears), dysacusis (loss of hearing)

Panuveitis: Vogt Koyanagi Harada Disease



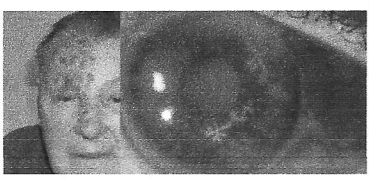
- Diagnosis: Fluorescein and ICG angiography, OCT scan, fundus hyperautofluorescence, lumbar puncture shows CSF pleocytosis (increased WBC's and protein)
- Treatment: Systemic corticosteroids, methotrexate, azathioprine, cyclosporine

Ocular Complications of HIV



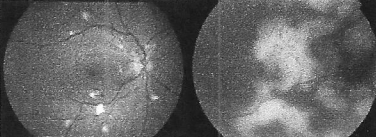
- Etiology: HIV incidence (37,600 new cases/year in 2014) declining due to HAART (highly active anti-retroviral therapy). Ocular complications occur in 70-80% HIV patients; increased risk when CD4 count drops to < 200 cells/cubic mm
- Ocular Findings: Kaposi's sarcoma, molluscum contagiosum

Ocular Complications of HIV




- Ocular Findings: Herpes zoster ophthalmicus, herpes keratitis

Ocular Complications of HIV



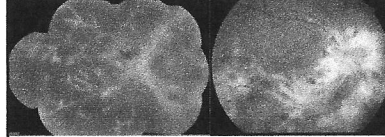
- Ocular Findings: HIV retinopathy, ocular syphilis, toxoplasmosis retinochoroiditis, ocular lymphoma,

Ocular Complications of HIV



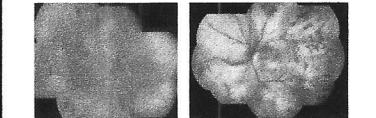
- Ocular Findings: fungal endophthalmitis

Ocular Complications of HIV



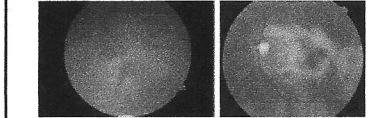
- Ocular Findings: Frosted branch angiitis, cytomegalovirus (CMV) retinitis

Panuveitis: ARN vs. PORN



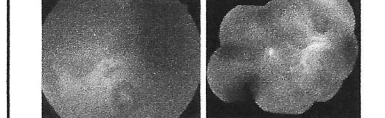
- ARN: Acute Retinal Necrosis (not immunocompromised)
- PORN: Progressive Outer Retinal Necrosis (immunocompromised or HIV)
- Etiology: Herpes (zoster or simplex) retinitis in both conditions

Panuveitis: ARN vs. PORN



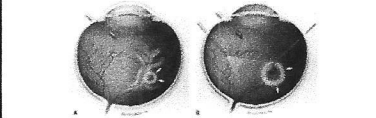
- Symptoms: Blurred vision, vitreous floaters, photophobia initially in one eye
- Ocular Findings: Rapidly progressive peripheral retinal necrosis with severe panuveitis and occlusive retinal vasculitis, retinal detachment, optic atrophy
- Diagnosis: PCR of intraocular fluids for herpes DNA

Panuveitis: ARN vs. PORN



- Medical therapy: Intravenous acyclovir x 14 days followed by oral valacyclovir x 3 months or longer
- Surgical Therapy: Prophylactic laser photocoagulation of large retinal breaks if retina not detached. Vitrectomy with endolaser and silicone oil tamponade if retina is detached.

Panuveitis: ARN vs. PORN



- Medical therapy: Intravenous acyclovir x 14 days followed by oral valacyclovir x 3 months or longer
- Surgical Therapy: Prophylactic laser photocoagulation of large retinal breaks if retina not detached. Vitrectomy with endolaser and silicone oil tamponade if retina is detached.

The Final Word

- History, history, history: Most cases of uveitis have a cause and the patient's medical history will give you the clues to finding it.
- Always dilate and examine both eyes: Anterior segment inflammation often has a posterior component that will indicate the cause.
- Be wary of simply treating with topical steroids without determining the cause of the uveitis: steroids suppress inflammation, delay making a diagnosis and, in some cases, can allow the underlying condition to worsen.

Thank you

Born: Dinuba, California, USA 4/19/47

College: Stanford University, Palo Alto, CA B.A. in Psychology 1965 - 1969

Medical School: Northwestern University, Chicago, IL 1969 - 1973

Internship: Beth Israel Medical Center, New York, NY 7/1973 - 6/1974

Residency: Ophthalmology, State University of New York, Downstate Medical Center, Brooklyn, NY 7/1974 - 6/1977

Fellowship: Retina-Vitreous Fellowship

Manhattan Eye, Ear and Throat Hospital
Cornell University Medical Center
New York, NY 7/1977 - 6/1978

Board Certified: American Board of Ophthalmology 1979

Medical Licensure: New York, U.S. – 8/1972 California, U.S. – 6/1975

Private Practice: Bay Area Retina Associates, California 1979 - Present

Assistant Clinical Professor of Ophthalmology

University of California San Francisco Medical Center
San Francisco, CA 1980 - present

Clinical Trials

Principal Investigator – VAM Study, Verteporfin and Age Related Macular Degeneration 1999 – 2000.
Sponsor – Novartis, Inc.

Principal Investigator – FOCUS Study for RhuFab V2 Phase II – 2002
Sponsor – Genentech, Inc.

Principal Investigator – MARINA Study for RhuFab V2 Phase III -2003
Sponsor – Genentech, Inc.

Principal Investigator – Ruboxistarin Study for Diabetic Macular Edema Phase III -2004 Sponsor –Eli Lilly, Inc.

Investigator – SCORE Study for BRVO/CRVO – 2004
Sponsor – NIH/NEI

Investigator – DRCR Studies for Diabetic Retinopathy – 2004
Sponsor – NIH/NEI

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Principal Investigator – HORIZON Study for RhuFab V2 Phase IIIb -2005
Sponsor – Genentech, Inc.

Principal Investigator – SAILOR Study for RhuFab V2 Phase IIIb -2005
Sponsor – Genentech, Inc.

Principal Investigator – ACU201-Cand5 Study Phase II -2005
Sponsor – Acuity Pharmaceuticals, Inc.

Investigator – PDEX Study-Combination Triple Therapy vs. Lucentis Monotherapy – 2006
Sponsor – Bay Area Retina Associates IST

Investigator – BRAVO Study for RhuFab V2 Phase III -2007
Sponsor – Genentech, Inc.

Investigator – CRUISE Study for RhuFab V2 Phase III -2007
Sponsor – Genentech, Inc.

Investigator – QUARK 003 Study for REDD14 siRNA Phase I -2007
Sponsor – Quark Pharmaceuticals, Inc.

Investigator – LUCEDEX Lucentis and Dexamethasone vs. Monotherapy Lucentis – 2008
Sponsor- Bay Area Retina Associates

Investigator- OASIS - Ocriplasmin for Treatment for Symptomatic Vitreomacular Adhesion Including Macular Hole- 2011
Sponsor-ThromboGenics

Investigator- SPECTRI - Lampalizumab Intravitreal Injections in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration- 2014
Sponsor-Hoffmann-La Roche

Investigator- STOMP - Short-Term Oral Mifepristone for Central Serous Chorioretinopathy. A Placebo-controlled Dose Ranging Study of Mifepristone in the Treatment of CSC, IST- 2015
Sponsor: Roger Goldberg, M.D.

Investigator- VAPOR 1–DE-120 Injectable Solution for Age-related Macular Degeneration- 2015
Sponsor: Santen, Inc.

Investigator- AVENUE - RG7716 Administered Intravitreally in Patients with Choroidal Neovascularization Secondary to Age-Related Macular Degeneration- 2015
Sponsor: Hoffmann-La Roche

Investigator- BOULEVARD - RO6867461 in Participants with Center-Involving Diabetic Macular Edema (CI-DME) Phase II - 2016
Sponsor: Hoffmann-La Roche

Principal Investigator- PAVE - DE-122 Injectable Solution for the Treatment of Refractory Exudative Age-related Macular Degeneration Phase I/II- 2015
Sponsor: Santen, Inc.

Investigator- OMASPECT - Lampalizumab in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration Who Have Completed a Roche-Sponsored Study – 2016
Sponsor: Hoffmann-La Roche, 2016