Pardon the Objection: Posterior Segment Update

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Diana Shechtman, OD, FAAO

Introduction
• Fast paced!
• Interactive!
  – Panel participation!
  – Audience participation!
• Apologies in advance!
  – The opinions and comments expressed in this lecture do not reflect those of the AOA or any sensible person

Disclosures
• FERRUCCI: Alcon, Arctic DX, Maculogix, Kemin, RetnaGene, ThromboGenics
• DUNBAR: Allergan, Arctic Dx, CZM, Sucampo; Co-Chair Education, Reed Exhibits
• POHL:
• SHECHTMAN: Allergan, Alcon, Arctic DX, B&L, CZM, Zeavision
What’s New in Imaging: AMD

- Advances in SDOCT
- Maculogics (dark adaption for AMD)

Advances in SD-OCT

- Progression analysis software
- Wider and deeper scans
  - Traditional scan area is 6 mm X 6 mm, now >12 mm scans
  - Software evolving to include whole posterior pole
- Greater density in the scans
- Higher resolution
The multi-dimensional platform for

- **Widefield Enface OCT**
- High-speed
- Multi-layered assessment of peripheral retina pathology
- Glaucoma
- Anterior segment analysis

Meeting the patient care needs of today... and the future.

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XR Avanti MCT with OCTA¹

OCT En face image
SSADA/OCTA Imaging

Detailed vasculature of the fovea without dye or contrast enhancement injection

Flow rate directly relates to appearance (brightness) of vessel in the image²

*Images courtesy of David Huang, M.D.
OHSU.

¹OCTA/SSADA is not yet commercially available.
Advanced RPE Analysis

• RPE Elevations: If the RPE is raised, a new proprietary algorithm for Cirrus maps and measures the area and volume of the elevations.

• Sub-RPE Illumination: If the RPE is absent or has lost integrity, a new proprietary algorithm for Cirrus can map and measure the affected area.

Esther: Geographic Atrophy

12/28/2010 vs. 1/18/2013

12/28/2010 1/18/2013
Drusen Analysis

Dark Adaptation Impairment in Patients with Age-related Macular Degeneration
Maculogics FDA Statement

• **Cleared** - 510(k) number K100954 - The AdaptDx™ is an AC powered, automated adaptometer (biophotometer) intended to measure the time for retinal adaptation after exposure to an adapting light.

AdaptDx

• Next-generation dark adaptometer for rapid, routine clinical use
• Simple, objective tool to measure dark adaptation as earliest functional correlate of AMD
• Two clinical protocols
  - 5 minute Rapid test
  - 20 minute Staging test

Dark Adaptation is an Established Marker of AMD

• Dark adaptation (DA) is severely impaired in AMD
• Biology of DA impairment is well understood and linked to breakdown of RPE/Bruch’s membrane complex
  - Impairment tracks with severity
  - Impairment is rod-mediated
• DA represents earliest functional correlate with AMD
• Traditional 90 minute test – too slow and impractical for clinical use

Diagnostic Sensitivity

Rapid Dark Adaptation Test Results

- Patients classified as having AMD if dark adaptation > 6.5 minutes
- High Sensitivity: correctly identified 90.6% of confirmed AMD cases
- High Specificity: correctly identified 90.5% of confirmed normal cases
- AMD cases exhibit no rod recovery of dark adaptation

AdaptDx™ Validation Study Results

<table>
<thead>
<tr>
<th>Screening Test - 5 minutes</th>
<th>Staging Test - 20 minutes</th>
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<tr>
<td>Log Sensitivity</td>
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<tr>
<td>Normal</td>
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<tr>
<td>Early AMD</td>
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<td>Intermediate AMD</td>
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<td>Advanced AMD</td>
<td>Advanced AMD</td>
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CHOROIDAL LESIONS
DIANA SHECHTMAN, OD, FAAO
When the NEVOMA PRESENTS
Choroidal nevus vs choroidal melanoma

30% of choroidal melanomas are small with <3mm thickness

So which is which & how do I know?

Tumor development

- Benign
  - Growth restricted to that area & no organ functional damage
- Malignant
  - Cell proliferation results in organ function damage. Cell proliferation may be due to:
    - lack of responses to normal apoptosis
    - genetic alteration cause by mutations
- Metastasis
  - Rapid growth with infiltration into other tissues

What are features of a choroidal nevus?

Choroidal Nevi: BENIGN proliferation (neoplams) of choroidal melanocytes

- 6-10% (blue mnt eye study) prevalence among whites
- No correlation w (+)FHx of any melanoma
- < 3 mm elevation
  - Typically FLAT
- < 3 DD in size
  - 90% are ≤2 DD; so if note
  - 3-5 DD it is questionable (NEVOMA)
20 yo asymptomatic
Disappears in RF
Ultrasound revealed no thickness
OCT shows no fluid

Nevus or melanoma?
What are the associated findings?

Nevus or melanoma?
Management-- 6:3:6

What do you think?
Is that LP or drusen?

In general, nevi rarely enlarge
Blue mountain Study (n = 160 nevi s/p with 5 yr follow up)
If no camera...document BORDERS
What are features of a choroidal melanoma?

Choroidal Melanoma

- Observe in white pts with a peak incidence in 50-60yo
- >3 mm elevation
- Usually >5mm in size
- Increase risk in light eyes, fair skin, propensity to burn, pts with numerous freckles

How do I know the choroidal lesion today is a melanoma tomorrow?

Growth over 7 ½ months
Melanomas grow RAPIDLY in height &/or diameter
Nevus or melanoma?

**To Find Small Ocular Melanoma**


**Management depends on # of features noted**

- No signs: annual exam
  - "<3% chance of growth"
- 1-2 signs: 4-6M f/u (sooner after initial Dx)
  - "38% chance of growth"
- ≥ 3 signs: consultation
  - "50% chance of growth over 5 yrs"

Orange pigment (lipofuscin) pathognomonic

**Why is a referral important with regards to a small melanoma?**

You save vision, you save eyes & you save...

**SAVE LIVES**

Highest incidence of metastatic detection is 1-3 yr s/p Dx of the choroidal melanoma

COMS 2001

\[ S: \text{<} 3 \text{ mm thickness (height) or } \text{<} 5-8 \text{ mm diameter} = 10\text{yr mortality rate } \text{<}10\% \\
M: 3-5 \text{ mm thickness (height) or } 10-15 \text{ mm diameter} = 10\text{yr mortality rate } \text{<}20\% \\
L: > 5 \text{ mm thickness (height) or } > 16 \text{ mm diameter} = 10\text{yr mortality rate } 40\% \\
\text{Diameter} = \text{largest linear tumor dimension (basal diameter)} \]
Why is identifying a small melanoma critical?
SIZE does matter

1. The 5-yr mortality rate after enucleation:
   - 16% small choroidal melanoma, 32% medium & 53% for large

2. 1 mm increase thickness = 5% increase risk of metastatic dz (10 yrs)

3. Despite direct tx of the choroidal melanoma, 30-50% of pts develop metastatic disease


What is the most common location of primary uveal melanoma to metastasize?

**Metastatic choroidal melanoma**

- Liver
- Brain
- Lungs
- Bone
- Breast
- Skin

Incidence of metastasis increase to 34% at 10 yr

>25% of patients with ocular melanoma will develop metastases within 5 yrs s/p Dx & 90% of those will metastasize to the liver

Median survival for a hepatic metastasis:
- 20% at 1 year
- 10% at 2 years
- <1% after 5 yrs, REGARDLESS OF TX

**BRVO**

MAYNARD POHL, OD, FAAO
Branch Retinal Vein Occlusion (BRVO)

- Thrombus formation at arteriovenous crossing
- Systemic hypertension commonly associated
- Age 60 – 70 most common

BRVO: Acute Findings

- Sectoral superficial hemorrhages
- Sectoral retinal edema
- Sectoral cotton-wool spots

BRVO: Chronic Findings

- Microvascular abnormalities
- Macular edema
- Intraretinal collaterals
- Sclerosis and sheathing of retinal vessels

Chronic BRVO
BVOS

• Branch Retinal Vein Occlusion Study Group, Archives Ophthalmology 1986; 104:34-41

BRVO: Laser Treatment Techniques

• Macular Grid Laser Photocoagulation: BRVO present for more than 3 months absence of foveal hemorrhage vision worse than 20/40 vision loss due to macular edema
Macular grid laser photocoagulation remains the criterion standard treatment of eyes with perfused macular edema secondary to BRVO.
BRVO: Laser Treatment Techniques

- Scatter Photocoagulation:
  - presence of neovascularization
  - presence of vitreous hemorrhage

BRVO: Other Treatment Techniques

- Laser-induced chorioretinal anastomosis
- Arteriovenous decompression (sheathotomy)
- Vitrectomy
- Intravitreal Kenalog (triamcinolone acetonide) – SCORE Study
- Ozurdex (0.7 mg dexamethasone intravitreal implant)
- Avastin, Lucentis, Eylea

Vascular Endothelial Growth Factor (VEGF)

- VEGF is a potent inductor of vascular permeability and intraocular neovascularization.
- Human aqueous levels of VEGF and interleukin 6 (IL-6) are correlated with the degree of retinal ischemia and the severity of macular edema in BRVO.
- Therefore, VEGF inhibition is a promising treatment modality for macular edema.

Clinical Evidence-Based Conclusions

- Timing of diagnosis and management of BRVO is important.
- Eyes with macular edema secondary to BRVO should be offered VEGF inhibition upon diagnosis to achieve the best possible visual outcome (BRAVO Study, HORIZON Trial, RETAIN Study).
- Eyes are eligible for laser after 3 months if hemorrhages have sufficiently cleared to allow safe laser treatment and if vision acuity remains worse than 20/40.
- Retinal nonperfusion is related to intravitreal VEGF levels and may result in loss of visual gains. The prevention of worsening retinal nonperfusion should be a treatment objective as important as the resolution of macular edema.
- Periodic fluorescein angiograms should be performed to monitor perfusion status.
Central Retinal Vein Occlusion (CRVO)

- Thrombus formation in retinal vein at lamina cribosa
- Etiology of thrombus formation unclear: arteriosclerosis, vasculitis
- Primary open angle glaucoma: 20% have POAG, 20% develop POAG

Systemic associations:
- CVD - 74%
- HTN - 57%
- DM - 34%

Risk factors include oral contraceptives and diuretics

90% of patients are over 50

Non-Ischemic (Partial) CRVO
Non-Ischemic CRVO

- 30+% convert to ischemic type (CVOS)
- < 10 dd of retinal non-perfusion (CVOS)

Ischemic (Complete) CRVO

Ischemic CRVO

- Marked optic disc, retinal, and macular edema
- Marked venous dilatation and tortuosity
- Many retinal hemorrhages, cotton-wool spots
- VA worse than 20/200
- Afferent pupillary defect

CRVO: Incidence of Neovascularization

- Non-Ischemic:
  - Any NV in < 5%
  - NV glaucoma in < 2%
- Ischemic:
  - Any NV in > 60%
  - NV glaucoma in 33%
CVOS

- *Central Retinal Vein Occlusion Study Group, Ophthalmology 1995; 102:1425-1444*

CVOS Conclusions

- Grid photocoagulation for macular edema: effective in decreasing retinal thickening but ineffective in improving VA
- Pan retinal photocoagulation to prevent neovascular complications: indicated only in eyes with apparent iris NV, angle NV, or ischemic eyes that cannot be followed monthly

CRVO: Other Advocated Treatments

- Aspirin
- Anti-inflammatory agents
- Isovolemic hemodilution
- Plasmapheresis
- Systemic anticoagulation with warfarin, heparin, and alteplase
- Fibrinolytic agents
- Systemic corticosteroids
- Intravitreal treatments – the standard of care

CRVO: Intravitreal Treatments

- Local anticoagulation with intravitreal injection of alteplase (Activase)
- Intravitreal injection of triamcinolone (Kenalog)
- Ozurdex intravitreal implant
- Intravitreal injection of Lucentis
- Intravitreal injection of Avastin
- Intravitreal injection of Eylea
Intravitreal Injection of Triamcinolone

- SCORE Study - CRVO Trial demonstrated effectiveness in resolving perfused macular edema and improving vision
- 1-mg dose and retreatment prn may be considered up to 12 months (preferred over 4-mg dose due to fewer adverse effects)

CRVO: Pre- and Post-OCT

- Pre-Injection: VA 20/400, thickness > 600 microns
- Post-Injection (6 weeks): VA 20/80, thickness 350 microns

Intravitreal Injection (IVI)

SCORE Study: Conclusion

- No difference in long-term outcome between triamcinolone injections and grid photocoagulation with BRVO.
- Ozurdex biogradable implant (Allergan, June 2009) is considered superior to triamcinolone as a delivery method, with fewer injections.
- Triamcinolone remains a viable option for patients with financial troubles.
Pre and Post Avastin Injection

Anti-VEGF Trials For RVO

• After 6 months of Lucentis therapy, between 55% and 61% of BRVO patients and 47% of CRVO patients gained at least 3 lines of BCVA (BRAVO and CRUISE studies).
• 12 month data: vision gained at 6 months continued after 6 months of subsequent prn dosage.
• From a strictly evidenced-based perspective, slightly better visual outcomes and huge safety profile, relative to steroids.
• Lucentis approved for treatment of macular edema following RVO in June 2010.
• Eylea approved for macular edema following CRVO in September 2012 (COPERNICUS and GALILEO trials)
• Anti-VEGF therapy ranks as the preferred first-line therapy for RVO.

Head-to-Head Studies in RVO

• COMO and COMRADE B – comparing Lucentis with dexamethosone IVT in BRVO patients
• COMRADE C – in CRVO patients
• RABAMES – comparing Lucentis, argon laser monotherapy, and Lucentis plus adjunctive argon laser therapy in BRVO patients (completed)
• BRIGHTER (EUDRACT 2011) – European studies with similar treatment arms

AMD TREATMENT
MARK DUNBAR, OD, FAAO
AMD: Management Options for Today and the Future

- **Dry AMD treatment**
  - Nutritional options
  - Targeting genetic factors

- **Wet AMD treatment**
  - Laser, PDT, Anti-angiogenic therapy
  - Prognosis for successful outcome is dependent on early diagnosis and treatment of CNV

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Ongoing Dry AMD Trials

<table>
<thead>
<tr>
<th>Company/Drug</th>
<th>Study</th>
<th>Treatment</th>
<th>Status</th>
</tr>
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<tbody>
<tr>
<td>Aerie</td>
<td>RELI</td>
<td>Monoclonal</td>
<td>Phase 1</td>
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<tr>
<td>Avanir</td>
<td>RELI</td>
<td>Monoclonal</td>
<td>Phase 2</td>
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<td>Tealys</td>
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<td>Monoclonal</td>
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Key Genes Involved in the Development of AMD

- **Complement**
- **Oxygen Metabolism**
- **Extracellular Matrix**
- **Cholesterol Metabolism**

Macula Risk NXG – 12 genes

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Lampalizumab (LAMP)

**Anti-factor D (Genentech)**

- A monoclonal antibody that inhibits Complement Factor D
- A rate-limiting enzyme involved in the alternative complement pathway
- A “key-driver” for the development of geographic atrophy
MAHALO Trial

- 129 pts with bilateral geographic atrophy randomized to assess the safety, tolerability, and activity of lampalizumab (LAMP)
- Biomarkers for complement factor H (CFH), C3, C2/CFB and CFI were also determined
- Participants, 60 - 89 y/o randomized to lampalizumab 10 mg or sham injections

### Treatment Interval | Lampalizumab, n | Sham, n
--- | --- | ---
Monthly | 43 | 21
Every other month | 44 | 21

MAHALO Trial

- A positive treatment effect was seen in the monthly lampalizumab group beginning at month 6, and was maintained through month 18 with primary and secondary imaging end points
- Subgroup analysis of monthly injections showed overall reduction in GA area in pts with a specific biomarkers was more than double that of the study cohort as a whole (44.0% vs. 20.4%)

Geographic Atrophy and Complement Factor I (CFI)

- 57% of genotype samples collected from 93 patients were positive for the CFI biomarker
- CFI biomarker is both prognostic for GA area progression and predictive for lampalizumab treatment response

ACQUIRED MACULOPATHIES
DIANA SHECHTMAN, OD, FAAO
MEDICATION toxicity

What was the previous tests used for plaquenil pts?

What are today’s tests?

Stages of HCQ/CQ Maculopathy

Early  Moderate  Advance

Protocol change in 2011
Revise Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy

Why were screening recommendations change

Typically retinopathy not observed until 5yrs s/p use of med
Analysis of 4,000 study 1.8% develop retinopathy s/p LONG term use of med

Risk of toxicity increases 5x s/p 7yrs of usage or at 1,000 GRAMS (1,000,000 mg) of exposure
Baseline
- detects any pre-existing maculopathy & other HR signs

Monitoring: determine if si/s maculopathy have occurred

LOW RISK

HIGH RISK

So when do YOU see the pt back?

Recommendations 2011 new protocols

Recommended Screening Procedures
- Dilated retinal examinations are important
- Automated visual field
  - White OCT threshold testing: Interpret with a lower threshold for abnormality, and retest if abnormalities appear.
  - If available, perform one or more of the following objective tests:

  - SD-OCT: Rapid test that can be done routinely, can show abnormalities very early, even before field loss
  - mfERG: Valuable for evaluating subtle or subtle visual field loss, may show damage earlier than visual field loss
  - FAF: May validate other measures of toxicity, can show abnormalities earlier than field loss

FAF shows decreased autoFL perifoveally: photoreceptor damaging denoted by increase FAF

What does the SDOCT damage Associated with toxicity look like?
Reading the OCT associated with plaquenil toxicity

Normal Patient

Where's the damage?

Plaquenil Patient

OCT:
Saucerazation & Sinkhole appearance

Displacement of the inner retinal structures toward the RPE with increase retinal atrophy

Chen et al. Clinical Ophthalmology 2010

28 BF

- CC: Decreased VA x 2 yrs
- PMHx: Lupus
- Meds: 8-9yrs
  - Plaquenil 200mg/QD
  - Pred 15mg / QD
- BCVA:
  - 20/20 OD, OS OU
- D/N

DFE: What's the Dx?
OCT: Does she have early toxicity?

WHEN DO YOU SEE HER BACK?
What do you communicate to the treating doctor?
What is HR pt?

WHAT IS HIGH RISK?

<table>
<thead>
<tr>
<th>Factors Increasing Risk of Retinopathy (HR)</th>
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<td>Duration of use</td>
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<tr>
<td>Cumulative Dose</td>
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<tr>
<td>Daily Dose</td>
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<tr>
<td>Age</td>
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<tr>
<td>Systemic Disease/High BMI</td>
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<tr>
<td>Ocular Disease</td>
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Daily Dosage

- **Daily Dosage**
  - **Standard dose**: 200mg/day or 400 mg/day
  - **Typically Rx as 6.5mg/kg**
  - **1 kg = 2.2 pounds**
    - 6.5mg/2.2 pounds = 2.95mg/pound
    - 400 mg HCQ/2.95 = 135 pounds
    - 400mg/Day is given to a 135lb pt (IDEAL weight)
  - **IDEAL weight**
    - At 5ft a woman weighs 100 lb women & a male weighs 110 men
    - 5lb added thereafter for every ft

OBESITY (BMI) & toxicity

- **Our pts are NOT at the ideal weight**
  - Pt with higher BMI is at risk because they are Rx based on 6.5mg/kg (& not based on LEAN muscle weight)
    - Hence, they are OVERDOSE
    - **DRUG is not** retained in Adipose (fat) tissue & thus, there are higher plasma levels of the drug.
  - Height recently has also been an issue—Hence, if you’re short, the standard Rx of 200 mg BID is TOO MUCH!
How do you deal with initial VF?
Do you repeat them initially q6M?
What does a plaquenil toxicity VFD look like?

How would you handle this case?

What do you communicate to the treating doctor?
Although there's a speculation that toxicity can be reversed if detected earlier, there's no conclusive evidence (no longitudinally studies). Yet, there's conclusive evidence that progression of toxicity occurs despite cessation of drug in many cases.

Marmor stated, “Goal is to catch changes at a very early stage when there’s just a minimal amount of damage. Then, when you stop the drug, the damage won’t progress enough to cross the fovea and affect reading vision.” The likelihood of toxicity is LOW—Dr. Marmor has seen only seen 10 cases in the past year.

Impact of the guidelines on today's practice!

**AJO 8/2013**

- n=183 pts came for f/u & 36 were evaluated for baseline
- Evaluated by 26 ophthalmologist & 3 ODs

**Results**

- 40% increase on health care cost
- 50% of doctors perform 6M rather than yrly f/u
- No additional pts discover with toxicity in accordance to new guideline.
- Incidence of toxicity remains at 1%, as noted in f/u pts
- No pts was followed at recommended guidelines of 5-year period after baseline (even if low-risk patient)

**Impact of the guidelines on today's practice!**

**AJO 8/2013**

- Small sample size
- No one perform FAF
- Pt’s height, weight, and daily dose were not determined in 1/3rd o the pts
Evidence-Based WHO Guidelines (2012)

- South Asian and Pacific Island populations now considered "high-risk" populations
- All Type 2 DM patients examined at diagnosis
- Type 1 DM patients examined at puberty
- Women with DM examined before pregnancy and during first trimester
- All DM patients regardless of degree of DR examined at least every 2 years
- Prevalence of blindness from DR is escalating in developing countries with a younger age of onset of DM
- Detection of referable retinopathy with single 45 degree non-mydriatic camera using trained operator with off-site grading by ophthalmologist, or trained ophthalmic medical officer or optometrist performing dilated fundus exam

Advanced Diabetic Retinopathy

Laser Photocoagulation & Vitrectomy in Diabetic Retinopathy

- Laser in Type 1 and Type 2 DM patients with NVE with vitreous heme, or with NVD with/without vitreous heme
- PRP considered in severe or very-severe NPDR
- Modified ETDRS macular laser in CSME when macular ischemia absent
- Vitrectomy in advanced DR: severe PDR with nonresolving vitreous heme or fibrosis, RD, or areas of retinal traction threatening macula
- Vitrectomy in persistent diffuse macular edema
Intraocular Steroids & Anti-VEGF Agents in PDR and CSME

- Macugen
- Avastin – BOLT study (monotherapy)
- Lucentis – RESOLVE study (monotherapy), READ-2 study (Lucentis vs laser vs combo)
- DCR.net – greatest improvement in VA is Lucentis and deferred laser (>6 mos after injection)
- NHMRC – consider anti-VEGF as an adjunct to laser and prior to vitrectomy
- Eylea
- Triamcinolone (IVTA) – in refractory DME, weighing risk vs benefit; as an adjunct to PRP in PDR

AMD GENETICS
MARK DUNBAR, OD, FAAO
Genetic analysis of 995 patients with intermediate (moderate) AMD who were in the original AREDS 1 study
Followed for 12 years
Evaluated the interaction of genetics and type of nutritional supplement on progression from moderate to advanced AMD

- Patients with genetically determined CFH high risk alleles, zinc was associated with increased progression to advanced AMD
- Patients with ARMS2 high risk alleles, zinc was associated with DECREASED progression to advanced AMD antioxidants worsened the outcome
- Patients with CFH risk alleles benefit from antioxidants without zinc but patients with ARMS2 risk alleles benefit from zinc without

49% derive more benefit from treatment other than AREDS

Estimate Probability of Progression

Recommended treatment: Antioxidants Alone
Genetic Testing and Recommending Nutritional Supplements

- Of the estimated 15 million Americans taking the AREDS formula, more than ten million should not be on either zinc or antioxidants
- Only about 23% of patients taking AREDS formula should be while the vast majority should not
- Genotype-directed therapy of the study population would have more than doubled the reduction in AMD progression rate compared to treatment with the AREDS formulation

VMT
DIANA SHECHTMAN, OD, FAAO
What are the common management options?

Option 1 is to REFER:
Given it may progress (associated with various complications)
But PPV is associated with a # of complications
WHAT ARE THE COMPLICATIONS ASSOCIATED WITH PPV?

Option 2 is to MONITOR
Given it may resolve on its own
WHEN DO YOU REFER?

LET US NOT FORGET THE BURDEN ON THE PT. Most surgeons advise pts to keep a head down ~7 days
Enzymatic Vitreolysis with Ocriplasmin for Vitreomacular Traction and Macular Holes

Peter Stalmans, M.D., Ph.D., Matthew S. Brintz, M.D., Arnd Gandorfer, M.D., Anselm Kampik, M.D., Aniz Girach, M.D., Stephen Pakola, M.D., and Julia A. Haler, M.D., for the MVI-TRUST Study Group

Jetrea has been commercially available Jan 2013 to tx symptomatic VMA

ABSTRACT

WHAT IS microplasmin
an active molecule similar to plasmin
Truncated form of active PLASMIN
recombinant protease with activity against fibronectin/lamin (components of VR interference)
functions as a thrombolytic agent causing an enzyme pharmacological induced vitreolysis
Nonsurgical PVD
The enzymatic agents alter the biochemistry of vitreous
Liquefaction of the vitreous occurs
LYSIS between vitreous cortex and ILM is the final outcome

Stalmans 2012

Truncated form of active PLASMIN recombinant protease with activity against fibronectin/lamin (components of VR interference) functions as a thrombolytic agent causing an enzyme pharmacological induced vitreolysis

Nonsurgical PVD

The enzymatic agents alter the biochemistry of vitreous
Liquefaction of the vitreous occurs
LYSIS between vitreous cortex and ILM is the final outcome

Stalmans 2012

Inclusion: VMT w VA ≤ 20/25 & OCT showing thickness
PPV advised if:
MD deemed it to be necessary s/p 1M
VA worsen by 2 lines or No improvement s/p tx
Primary outcome

Among those pts that resolved s/p injection, 73% were w/I 1st week.

% of the drug is short

20/32 20/32 20/20
20/25 20/16 20/20

Case Sample: MIVI-Study pt

20/25 20/16 20/20

Day 28 Month 3 Month 6

Abbreviations: Ant., anterior; VA, visual acuity.


Treatment-related Adverse Events
Postinjection Day 0 to 7

0 5 10 15
Retinal Detachment Retinal Tear

0 3 6
Pre-vitrectomy Occurrences

0 2 4 6
All Occurrences

Proportion of Patients with Retinal Tear or Retinal Detachment

0 2 4 6

Retinal Detachment Retinal Tear

Placebo N=187 Ocriplasmin N=465

10% adverse affects. Most effects noted within the 1st 7 days due to localize injection. They were transient and after 8d the adverse effects were minimal & equal b/t tx & placebo.
Resolution of VMA at Day 28
By Predictors of Response
Ray 2012

Increasing the # of (+) features was associated with increase odds VMA resolution
50% respond rate with > 3 predictive factors
Singh Ophthal 2013

Terminology: VMA/VMT
Sub classified by size of adhesion
Focal vs broad

Case Sample: MIVI-Study pt
Baseline 7 days
Day 28 Month 3 Month 6

Note primary outcome was PVD w VA improvement as SECONDARY outcome

SO DO YOU REFER FOR JETREA?
 IF YES, WHEN?
Thank you!