MACULAR DEGENERATION UPDATES

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VitreoRetinal Surgery | Loma Linda, California
Financial Disclosures

• NONE
Overview

• Dry AMD
• Wet AMD
• Current Therapies
• Future Therapies
• ForeseeHome
AMD Demographics

• NEI: 15 million Americans have AMD
• Leading cause of vision loss in adults 60 or older
Risk Factors

• Family history of the disease
• Smokers
• Obese
• High blood pressure
• More common in Caucasians
• Over 50 years old
Age-Related Macular Degeneration (AMD)

Early
- Multiple small or a few intermediate drusen

Intermediate
- Extensive intermediate drusen

Advanced
- Choroidal Neovascularization
- Geographic Atrophy
- Subretinal Fibrosis
AMD

• Presence of at least intermediate size drusen (>63 um)
AMD

- Presence of at least intermediate size drusen (>63 μm)
  - 125 μm is the width of an average large vein at the disc margin
AMD

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• RPE changes (hypo/hyperpigmentation)
AMD

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  • 125 μm is the width of an average large vein at the disc margin
• RPE changes (hypo/hyperpigmentation)
• Reticular pseudodrusen
AMD

- Presence of at least intermediate size drusen (>63 μm)
  - 125 μm is the width of an average large vein at the disc margin
- RPE changes (hypo/hyperpigmentation)
- Reticular pseudodrusen
- Presence of any of the following
  - GA
  - Choroidal Neovascularization
  - Polypoidal choroidal vasculopathy
  - Retinal angiomatous proliferation
Early AMD

- Multiple small drusen (<63 um)
- A few intermediate drusen (63-124 um)
- Mild RPE abnormalities
Intermediate AMD

• Numerous intermediate drusen

• At least one large druse (>125um)

• Geographic atrophy not involving the center of fovea
Advanced AMD

• GA involving foveal center
Advanced AMD
CNV
Advanced AMD
Serous and/or hemorrhagic detachment of neurosensory retina or RPE
Advanced AMD
Retinal Hard Exudates
(2/2 chronic intravascular leakage)
Advanced AMD
Subretinal and sub-RPE fibrovascular proliferation
Advanced AMD
Disciform Scar
Simplified Severity Scale
Right Eye
  - Large Drusen
    - Yes = 1
    - No = 0
    - Yes = 1
  - Pigment Changes
    - No = 0
    - Yes = 1

Left Eye
  - Large Drusen
    - Yes = 1
    - No = 0
  - Pigment Changes
    - No = 0
    - Yes = 1

Large Drusen and Pigment Changes
Patient Severity Score = 4 Risk Factors
## Five-Year Rates of Advanced AMD (In One or Both Eyes for Patients With Both Eyes at Risk)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Patients Without Advanced AMD in Either Eye at Baseline</th>
<th>Patients with Advanced AMD in One Eye at Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. at Risk</td>
<td>No.</td>
</tr>
<tr>
<td>0</td>
<td>1466</td>
<td>6</td>
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<tr>
<td>1</td>
<td>635</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>455</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>328</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>317</td>
<td>150</td>
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</table>
Dry AMD Treatment:

• Antioxidant vitamin and mineral supplementation as per AREDS/AREDS2 trials should be considered in patients with intermediate or advanced AMD
<table>
<thead>
<tr>
<th>Supplements</th>
<th>Amount (QD)</th>
<th>Comments (percentage DV*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AREDS2</td>
<td>AREDS</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>500 mg</td>
<td>500 mg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>400 IU</td>
<td>400 IU</td>
</tr>
<tr>
<td>Zinc</td>
<td>80 mg</td>
<td>80 mg</td>
</tr>
<tr>
<td>Copper</td>
<td>2 mg</td>
<td>2 mg</td>
</tr>
<tr>
<td>Beta-carotene</td>
<td>X</td>
<td>15 mg</td>
</tr>
<tr>
<td>Lutein</td>
<td>10 mg</td>
<td>X</td>
</tr>
<tr>
<td>Zeaxanthin</td>
<td>2 mg</td>
<td>X</td>
</tr>
</tbody>
</table>

*Percentage DV based on a 2000-calorie diet, **DV not established.
DV=Daily value; AREDS2=Age-related eye disease study 2; AREDS=Age-related eye disease study
Dry AMD Treatment:

• Eat a well balanced diet, rich in fruit, vegetables, Mediterranean diet
9 Health Benefits of a Vegetarian Diet
Dry AMD Treatment:

• Exercising 3x/week can decrease risk of wet AMD by 70%
Dry AMD Possible Future Treatments:

• Lampalizumab
• APL-2 (complement C3 inhibitor): Pending Phase 3
• Brimonidine
• Atorvastatin
• Photomodulation
• Minocycline
Pathways and Therapeutic Targets in Dry AMD

1. Visual cycle toxic by-products
   - Visual cycle modulators

2. Inflammation, complement, and ECM
   - mTOR inhibitors
   - Complement inhibitors
   - MMP inhibitors

3. Lipoprotein accumulation
   - LDL-lowering drugs

4. Beta-amyloid accumulation
   - Anti-amyloid beta

5. Oxidative stress
   - Anti-oxidants
   - Neuroprotectant

6. Choriocapillaris atrophy
   - Choroidal perfusion enhancers

7. RPE and photoreceptor loss
   - Stem cell therapy
   - Neurotrophins
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Sponsor</th>
<th>Trial subjects</th>
<th>Clinical phase</th>
<th>Clinical trial identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimetazidine</td>
<td>Anti-ischemic agent with cytoprotective effects (oral)</td>
<td>Institut de Recherches internationales Servier</td>
<td>Drusen in study eye, wet AMD in follow eye</td>
<td>Phase III</td>
<td>ISRCTN99532788 (completed - not published)</td>
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<tr>
<td>MC-1101</td>
<td>Increase choroidal blood flow (topical)</td>
<td>MacuCLEAR</td>
<td>Dry AMD</td>
<td>Phase II/III</td>
<td>NCT02127463 (ongoing)</td>
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<tr>
<td>NT-501: encapsulated CNTF</td>
<td>Neuroprotection: rescues photoreceptors from degeneration (intravitreal)</td>
<td>Neurex Pharmaceuticals</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT00447954 (completed at April, 2011)</td>
</tr>
<tr>
<td>Brimonidine tartrate</td>
<td>Neuroprotection: alpha-2 adrenergic receptor agonist (intravitreal)</td>
<td>Allergan</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT00658619 (completed at March, 2013)</td>
</tr>
<tr>
<td>Tandosporine (AL-8309B)</td>
<td>Neuroprotection: 5-HT1A receptor agonists (selective serotonin 1A receptor agonist) (topical)</td>
<td>Alcon</td>
<td>Geographic atrophy</td>
<td>Phase III</td>
<td>NCT00890097 (terminated at June 2014)</td>
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<tr>
<td>RN6G</td>
<td>Neuroprotection: binds and eliminates amyloid β (IV)</td>
<td>Pfizer</td>
<td>Geographic atrophy</td>
<td>Phase I</td>
<td>NCT00877032 (completed - not published at March, 2015)</td>
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<tr>
<td>GSK 933776</td>
<td>Neuroprotection: binds and eliminates amyloid β (INF)</td>
<td>GSK</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT01342926 (ongoing)</td>
</tr>
<tr>
<td>Fenretinide</td>
<td>Visual cycle inhibitors: Retinol analog inhibits binding of retinol (oral)</td>
<td>Sirion Therapeutics</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT00429936 (completed at June 2010)</td>
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<tr>
<td>Emixustat HCl (ACU-4429)</td>
<td>Visual cycle inhibitors: Nonretinoid inhibits isomerization of retinol (oral)</td>
<td>Acucela</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT01002950 (completed at Feb, 2014)</td>
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<tr>
<td>SEATTLE</td>
<td></td>
<td></td>
<td></td>
<td>Phase II/III</td>
<td>NCT01802866 (ongoing)</td>
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</tbody>
</table>

CNTF=Ciliary neurotrophic factor; IV=Intravenous; AMD=Age-related macular degeneration; INF=Interferon; GSK=GlaxoSmithKline
<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanism of action</th>
<th>Sponsor</th>
<th>Trial subjects</th>
<th>Clinical phase</th>
<th>Clinical trial identifier</th>
<th>IV=Intravenous; AMD=Age-related macular degeneration</th>
</tr>
</thead>
<tbody>
<tr>
<td>POT-4/AL-78898A</td>
<td>Inhibits complement component 3 (intravitreal)</td>
<td>Potentia/alcon</td>
<td>Wet AMD Advanced neovascular lesions</td>
<td>Phase I</td>
<td>NCT00473928 (completed at March, 2010)</td>
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<tr>
<td>ARC1905</td>
<td>Aptamer against complement component 5 (intravitreal)</td>
<td>Ophthotech</td>
<td>Geographic atrophy and/or drusen</td>
<td>Phase I</td>
<td>NCT00935883 (completed at November, 2013)</td>
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<tr>
<td>Eculizumab</td>
<td>Monoclonal Antibody against complement component 5 (IV)</td>
<td>Alexion</td>
<td>Geographic atrophy and/drusen</td>
<td>Phase II</td>
<td>NCT00935883 (completed at January, 2015)</td>
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<tr>
<td>FCFD4514S</td>
<td>Fab derived from a monoclonal antibody against complement factor D (intravitreal)</td>
<td>Genetech/Roche</td>
<td>Geographic atrophy</td>
<td>Phase I</td>
<td>NCT00973011 (completed at February, 2012)</td>
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<tr>
<td>Glatiramer acetate (Copaxone, Teva)</td>
<td>Induces glatiramer acetate-specific suppressor T-cells and downregulates inflammatory cytokines (subcutaneous)</td>
<td>Kaplan Medical Center New York Eye and Ear Infirmary</td>
<td>Drusen</td>
<td>Phase II, III</td>
<td>NCT00466076 (unknown April, 2007) NCT00541333 (suspended at May 2013)</td>
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<tr>
<td>Fluocinolone acetonide (iluvien)</td>
<td>Glucocorticoid-mediated Suppression of inflammation (intravitreal)</td>
<td>Alimera sciences</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT00695318 (terminated at May 2015)</td>
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<tr>
<td>LFG 316</td>
<td>Inhibits complement component 5 (intravitreal)</td>
<td>Novartis</td>
<td>Geographic atrophy</td>
<td>Phase II</td>
<td>NCT01527500 (completed at December, 2015)</td>
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<tr>
<td>TA 106</td>
<td>Antigen-binding fragment from a monoclonal antibody against complement factor B</td>
<td>Taligen Therapeutics</td>
<td>Dry AMD</td>
<td>Preclinical</td>
<td>None</td>
<td></td>
</tr>
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</table>
GA trials:

• Prevention of progression to GA
• Slow down the growth of GA
• Bringing back whatever has been lost in GA
Wet AMD

- Although around 80% of AMD patients have dry AMD, the wet form is responsible for 90% of severe vision loss associated with AMD.
Advanced AMD
Major Public Health Problem

Number of Individuals With Neovascular AMD or Geographic Atrophy (millions)

- 2000: 1.75 million
- 2020: 2.95 million

No. of individuals (millions)
Wet AMD

• The hallmark feature of the wet or neovascular form of age-related macular degeneration (nvAMD) is the presence of choroidal (or retinal) neovascularization (CNV).
Wet AMD

• If left untreated, CNV may result in significant central vision loss due to complications including exudation, leakage, and ultimately subretinal fibrosis causing remarkable photoreceptor loss.
Treatment of Wet AMD

• Pegaptanib (Macugen: VISION trials)
• Ranibizumab (Lucentis: MARINA/ANCHOR)
• Afibercept (Eylea: VIEW)

• Off label: Bevacizumab (Avastin: CATT)
Goal of Treatment:

• Maintain disease remission while minimizing side effects and treatment burden
Treatment Modules:

• Monthly
  • Continuous fixed monthly regimens associated with best visual outcomes
Treatment Modules:

• Monthly
  • Continuous fixed monthly regimens associated with best visual outcomes

• PRN
  • Failed to preserve vision gains comparable to monthly gains (CATT)
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• Monthly
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• Treat and Extend
Treatment Modules:

• Monthly
  • Continuous fixed monthly regimens associated with best visual outcomes

• PRN
  • Failed to preserve vision gains comparable to monthly gains (CATT)

• Treat and Extend
  • 65% of US ASRS members prefer this method
Treatment Modules:

• Monthly
  • Continuous fixed monthly regimens associated with best visual outcomes

• PRN
  • Failed to preserve vision gains comparable to monthly gains (CATT)

• Treat and Extend
  • 65% of US ASRS members prefer this method
  • Goal is to establish an individual patient’s optimal interval since many eyes show predictable pattern of recurrence
    • 10-20% need monthly
    • 10-20% show extended disease quiescence
Treatment Modules:

Some may require injections at shorter than q4 week intervals
Wet AMD Future Therapies:

• Long-Acting Anti-VEGFs
• Sustained Delivery Treatments
• Topical Treatments
• Oral-Anti-VeGFs
• Gene Therapy
<table>
<thead>
<tr>
<th>Compound</th>
<th>Company</th>
<th>Stage of Development</th>
<th>Structure/Mechanism of Action</th>
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<tbody>
<tr>
<td>Brocicizumab</td>
<td>Novartis</td>
<td>Phase III</td>
<td>small MW humanized single-chain Fab anti-VEGF-A</td>
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<tr>
<td>Abicipar pegol</td>
<td>Allergan</td>
<td>Phase III</td>
<td>DARPin antagonist of VEGF-A</td>
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<td>OPT-302</td>
<td>Ophthea</td>
<td>Phase IIb</td>
<td>anti-VEGF-C/VEGF-D</td>
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<tr>
<td>Pegpleranib (Fovista)</td>
<td>Ophthotech</td>
<td>Phase III</td>
<td>anti-PDGFR-B/anti-VEGF co-formulation</td>
</tr>
<tr>
<td>Rituximab-atlifercept</td>
<td>Regeneron</td>
<td>Phase II</td>
<td>dual TKI of VEGF-A/PGDF</td>
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<tr>
<td>DE-120</td>
<td>Santen</td>
<td>Phase II</td>
<td>Ang-2/VEGF-A mAb co-formulation</td>
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<tr>
<td>Nesvacumab-atlifercept</td>
<td>Regeneron</td>
<td>Phase II</td>
<td>bispecific Ang-2/VEGF-A antibody</td>
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<td>RG7716</td>
<td>Roche</td>
<td>Phase II</td>
<td>Tie-2 receptor activation (via VE-PTP inhibition)</td>
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<td>ARP-1536</td>
<td>Aerpio</td>
<td>Preclinical</td>
<td>oral anti-VEGF-A/PGDFR</td>
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<td>X-82</td>
<td>Tyrogenex</td>
<td>Phase II</td>
<td>oral anti-VEGF-A/PGDFR</td>
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<td>Pazopanib</td>
<td>GlaxoSmithKline</td>
<td>Phase II</td>
<td>TKI of VEGF-A/PGD</td>
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<td>Bayer Healthcare</td>
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<td>TKI of VEGF-A/PGD</td>
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<td>LHA510</td>
<td>Alcon</td>
<td>Phase II</td>
<td>VEGF-A inhibitor</td>
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<td>Ranibizumab PDS</td>
<td>Genentech</td>
<td>Phase II</td>
<td>refillable port of VEGF-A mAb</td>
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<td>GB-102</td>
<td>GrayBug Vision</td>
<td>Preclinical</td>
<td>bioerodible nanoparticles encapsulate TKI of VEGFR/PGDFR</td>
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<td>NT-503 ECT</td>
<td>Neurotech</td>
<td>Phase II terminated</td>
<td>VEGF-A receptor fusion protein</td>
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<td>Hydrogel depot</td>
<td>Ocular Therapeutix</td>
<td>Preclinical</td>
<td>sustained-release anti-VEGF-A</td>
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<td>Durasept</td>
<td>pSivida</td>
<td>Preclinical</td>
<td>TKI of VEGF-A/PGD</td>
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<td>ENV1305</td>
<td>Envisia Therapeutics</td>
<td>Preclinical</td>
<td>sustained-release anti-VEGF-A</td>
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<td>AVA-101</td>
<td>Adverum Biotechnologies</td>
<td>Phase Ila results were mixed</td>
<td>AAV sFLT</td>
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<td>AAVA-201</td>
<td>Adverum Biotechnologies</td>
<td>Preclinical</td>
<td>AAV sFLT</td>
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<td>ADVM-022/ADV-032</td>
<td>Adverum Biotechnologies</td>
<td>Preclinical</td>
<td>AAV encoding anti-VEGF-A cDNA</td>
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<td>AAV2-sFLT01</td>
<td>Genzyme (Sanofi)</td>
<td>Phase I</td>
<td>AAV sFLT</td>
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<td>RGX-314</td>
<td>Regenxbio</td>
<td>Preclinical</td>
<td>AAV8 encoding anti-VEGF-A</td>
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<tr>
<td>Retinosstat</td>
<td>Oxford Biomedica</td>
<td>Phase II</td>
<td>PLAV encoding endostatin and angiostatin</td>
</tr>
</tbody>
</table>
Wet AMD Take Home Point

• It is a chronic disease
• Meds might not all be equal
• Recurrence is different per patient
Amsler Grid (recording chart)
ForeSee Home
ForeseeHome FDA Indication for Use

• ForeseeHome is intended for use in the detection and characterization of **central and paracentral metamorphopsia** (visual distortion) in patients with age-related macular degeneration.
ForeseeHome FDA Indication for Use

The ForeseeHome AMD Monitoring Program is available by prescription only to dry AMD patients at risk of developing CNV.
Analyses from 5 Landmark Studies have Demonstrated that Several Baseline Characteristics Predict VA Outcomes

<table>
<thead>
<tr>
<th>Baseline Measure</th>
<th>CATT 1 year</th>
<th>HARBOR 1 year</th>
<th>MARINA 2 years</th>
<th>ANCHOR 1 year</th>
<th>TAP/VIP 1 year</th>
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</thead>
<tbody>
<tr>
<td>CNV lesion size/leakage area</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<td>BCVA</td>
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<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>Age</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<td>SRF presence</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
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<tr>
<td>RPE elevation</td>
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<td></td>
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<td>Occult CNV</td>
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<td></td>
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<td>GA presence</td>
<td>✔</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Foveal thickness</td>
<td>✔</td>
<td></td>
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</table>
“The detection of CNV before there is a large loss of vision remains important even in the era of highly effective treatment.” – CATT Study Group
Smaller, younger lesions demonstrated a better VA outcome at 1 year

Irreversible vision loss can occur when there is a delay in diagnosis and treatment.
A limited number of newly diagnosed CNV eyes are detected early.

Proportion of Eye(s) \( \geq 20/40 \) at CNV Diagnosis

*All but CATT included eyes with VA of 20/20 or worse (CATT included \( \leq 20/25 \)*
## Core Technology Based on Hyperacuity

**Greater sensitivity for detecting minute vision changes in AMD**

<table>
<thead>
<tr>
<th>Visual acuity (resolution)</th>
<th>Hyperacuity (Vernier acuity)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Image of E and mE" /></td>
<td><img src="image2" alt="Image of aligned circles" /></td>
</tr>
<tr>
<td>JND*: 30-60”</td>
<td>JND*: 3-6”</td>
</tr>
</tbody>
</table>

- **Two-points discrimination**
  - Low sensitivity
  - Age-dependent
  - Blur-dependent

- **Detection of misaligned objects**
  - High sensitivity
  - Resistant to age
  - Insensitive to blur

JND*: just noticeable difference
Preferential Hyperacuity Perimetry (PHP)
Technology is Based on Vernier Acuity

- The human ability to perceive minute differences in the relative spatial localization of two objects
- The brain is exceptionally sensitive to such deviation
- In the fovea, hyperacuity ability is in the range of 3-6” (sec) of arc (~10x better than standard acuity)
Ability to assess progression of AMD based on principle of a pathological distortion competing with an “artificial” distortion introduced in the stimuli of the visual function test. Pathological > Artificial = Possible CNV = Alert

PHP Home-based Technology: ForeseeHome®

Can detect changes in metamorphopsia often before the patient notices any visual symptoms.

First FDA-cleared, Medicare-covered daily home monitoring system for intermediate AMD patients at risk for progression to CNV.
An alert is generated by MULTIPLE CROSSES over the threshold. A single test would not trigger an alert.
The ForeseeHome® Process

Patient completes the brief non-invasive test daily; ~3 mins per eye.

A baseline reference score and map is generated within the first few weeks; daily test results are sent to the Notal Data Monitoring Center.

When a statistically significant change is detected, Doctor is alerted and follow up plan is initiated.

Physicians are sent monthly reports and can view patient data via a website. The reports can be used as a follow-up tool during clinic visits.

MORE ABOUT THE ALERT…

- The ordering physician receives the alert (standard protocol)
- In addition, alerts can be sent simultaneously to the ordering physician AND patients by physician consent. The patient is alerted that a statistically significant change in testing has occurred, and is asked to contact their eyecare provider as soon as possible.
The HOME Study
Does home monitoring with PHP (ForeseeHome) plus standard care result in earlier detection of progression to CNV when compared to standard care alone?

**Study Methods & Demographics**

- **Inclusion**: Dry AMD patients with 3 or 4 risk factors per AREDS scale
  - ≥ 1 large druse (≥125 microns)
  - VA ≥ 20/60
  - No CNV, scarring, or central GA in the study eye(s)

- **1520 patients** enrolled from 44 AREDS2 centers
**Study Design**

- **PHP + Standard Care (PHP ARM)**
  - (n=763)

- **Standard Care**
  - (n=767)

- **Suspected CNV:**
  - Alert
  - Symptoms
  - Scheduled Visit

- **Study Visit:**
  - Biomicroscopy, BCVA, OCT, FA

- **MD Confirmed CNV**

- **Met Primary Endpoint**

- **Suspected CNV:**
  - Symptoms
  - Scheduled Visit

- **Study Visit:**
  - Biomicroscopy, BCVA, OCT, FA

- **MD Confirmed CNV**

- **Met Primary Endpoint**
Outcome Measures

**Primary Outcome:** Change in VA from baseline to time of incident CNV

- **Secondary Outcomes**
  - Additional VA outcomes (i.e. proportion maintaining ≥20/40 at diagnosis)
  - Sensitivity and specificity (“First to alert” and false positive alert rate)
  - Lesion characteristics at the time of CNV diagnosis – not reported until full dataset available
As a result of earlier detection, CNV EVENTS ACCUMULATED FASTER in the PHP arm vs. STD care.

CNV events confirmed by physician at time point when DSMC recommended study termination for efficacy

ITT population: Includes all assigned to PHP whether using or not.
Change in VA Score from Baseline at CNV Detection

<table>
<thead>
<tr>
<th>PHP ARM</th>
<th>9 LETTER LOSS</th>
<th>4 LETTER LOSS</th>
<th>3 LETTER LOSS</th>
<th>3 LETTER LOSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT</td>
<td>P=0.021</td>
<td>P=0.007</td>
<td>P=0.005</td>
<td></td>
</tr>
<tr>
<td>PP1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5-6 LETTER DIFFERENCE
between PHP arm & STD care

ITT population: Includes all assigned to PHP whether using or not
PP population: (1) Real life after est. baseline; (2) Minimal recommended practice
Proportion of Eyes Maintaining ≥20/40 at CNV Detection

<table>
<thead>
<tr>
<th>Group</th>
<th>Proportion (≥20/40)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STD Care N=18</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>ITT N=40</td>
<td>87%</td>
<td>0.014</td>
</tr>
<tr>
<td>PP1 N=32</td>
<td>91%</td>
<td>0.005</td>
</tr>
<tr>
<td>PP2 N=29</td>
<td>94%</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Up to 50% increase in patients within the PHP arm vs. STD care

ITT population: Includes all randomized to PHP arm whether using or not
PP population: (1) using device at the time of the event; (2) Recommended testing of at least 2 times per week, and using at the time of the event
Performance of PHP

79% of PHP arm participants had no false alerts over the period of 1.4 years (study duration)

An average of 1 false alert may occur in 1 patient over 4 YEARS of continual testing for that patient
ForeseeHome diagnoses CNV with smaller lesion size

Lesion Size (DA)

- PIER: 4.2* (Mean)
- CATT: 2.9* (Mean)
- IVAN: 3.7* (Mean)
- HOME - Stnd Care: 0.7+ (Median)
- HOME - Device ITT: 0.23+ (Median)

* Mean  + Median
Incorporation of ForeseeHome facilitates earlier detection of CNV in a greater proportion of patients.

Baseline VA at CNV Diagnosis
Proportion of eye(s) VA ≥20/40

<table>
<thead>
<tr>
<th>Study</th>
<th>Proportion VA ≥20/40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olsen 2000</td>
<td>22%</td>
</tr>
<tr>
<td>Acharya 2005</td>
<td>17%</td>
</tr>
<tr>
<td>Fong 2008</td>
<td>13%</td>
</tr>
<tr>
<td>CATT* 2009</td>
<td>36%</td>
</tr>
<tr>
<td>IVAN 2010</td>
<td>41%</td>
</tr>
<tr>
<td>Wills T&amp;E 2013</td>
<td>14%</td>
</tr>
<tr>
<td>HOME Control 2013</td>
<td>62%</td>
</tr>
<tr>
<td>HOME Device PP2 2013</td>
<td>94%</td>
</tr>
</tbody>
</table>

*All but CATT included eyes with VA of 20/20 or worse (CATT included ≤20/25)
On April 30, 2013, the DSMC reviewed the study results and concluded that study eyes at risk of AMD progression presented to their study sites with SIGNIFICANTLY BETTER VISION WHEN THEIR NEOVASCULAR AMD DEVELOPMENT WAS DETECTED BY THE FORESEEHOME DEVICE as compared to standard monitoring.

Therefore, the DSMC UNANIMOUSLY RECOMMENDED EARLY TERMINATION OF THE STUDY AS THEY WERE CONFIDENT THAT THE STUDY HAD MET ITS PRIMARY OBJECTIVE; namely, demonstrating that eyes at high risk of progression to neovascular AMD can be identified with better levels of vision when they are detected by use of the home monitoring device as compared to standard methods.
Medicare Coverage for ForeseeHome

Achieved November 2015

Dry Intermediate AMD patients at High Risk for Progression to CNV
BCVA of 20/60 or better

ICD-10 Codes:

- H 35.31 1 2 (Dry Intermediate, Right Eye)
- H 35.31 2 2 (Dry Intermediate, Left Eye)
- H 35.31 3 2 (Dry Intermediate, Bilateral)

Candidates may include:

- Dry AMD eyes (bilateral) with intermediate sized drusen and hyperpigmentation
- Dry AMD in one eye (testing eye) and Wet AMD in fellow eye
WHY DO I USE PHP?

- Provides the highest quality care I can provide my intermediate dry AMD patients
- Increases likelihood that my patients will be able to remain independently able to drive, read, and enjoy their quality of life
- Reinforces that they are at risk for wet AMD and provides a better understanding of their disease

WHO ARE THE IDEAL CANDIDATES?

- Intermediate AMD eye(s) at risk for progressing to CNV
- 20/60 BCVA or better in monitoring eye(s)
- No CNV, scarring or central GA in monitoring eye(s)
- In SHORT: Intermediate dry AMD; those recommended an AREDS2 vitamin formulation
Thank you

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