Innovations in Eye Care
A Rapid-Fire Presentation
What's Here, What's Coming, and What You Need to Know

Greg Caldwell OD, FAAO
Mike Cymbor, OD, FAAO
James Deom, OD
Tom Kislan, OD

Disclosures - Greg Caldwell, OD, FAAO
Will mention many products, instruments and companies during our discussion.
- I don’t have any financial interest in any of these products, instruments or companies.
- Pennsylvania Optometric Association - President 2010
- POA Board of Directors 2006-2011
- Thank you to the members and those who ask.
- I never used or will use my volunteer positions to further my lecturing career
- Lectured for: Shire, BioTissue, Optovue
- Advisory Board: Allergan
- Evolve: PA Medical Director

Disclosures – Mike Cymbor, O.D., F.A.A.O.
- POA Awards Committee
- Speakers Bureau for Optovue, Bausch and Lomb

Disclosures - James Deom, OD
- Allergan
- Mibo Medical
- Sun Pharmaceuticals
- Biotissue
- Diopsys
- Valley Contax

Disclosures Thomas P. Kislan, OD
- Alcon
- Allergan
- Biotissue
- B+L
- Hoya
- Katena
- MiboMedical
- PRN
- RPS
- Shire
- Tear Lab

Learning Objectives
- Introduce the innovation to the clinician in each of the topic areas
- Discuss how the innovation will impact the diagnosis and treatment in eye care
- Reveal the benefit of embracing the innovation
- Demonstrate how it will impact patient care
- Demonstrate how to integrate the innovation into the clinician’s practice
- Enhance the clinician’s knowledge of selected innovations that impact eye care

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Course Description

This course will reveal, feature, and spotlight innovations in eye care that will impact every optometrist:
- Ocular surface/dry eye
- Posterior Segment Disease
- Drug delivery systems
- Surgery
- Refractive Surgery

Bioengineered Silk Grafts for Sub-Specialty Ophthalmic Surgical Procedures

REGULATORY
SILKTEK™ TECHNOLOGY HAS BEEN USED IN THE HUMAN BODY FOR DECADES, FIRST AS SILK SUTURES AND MOST RECENTLY AS MESH MATERIAL FOR HERNIA REPAIR.
THE COMPANY HAS RECEIVED A REGULATORY EVALUATION INDICATING THE OPHTHALMOLOGY APPLICATION WILL BE COVERED UNDER THE CLASS ONE DEVICE LABELING BY THE FDA.
CE Mark Filing Is In Progress

BACKGROUND
WORLD'S FIRST SILK BIOENGINEERED MATERIAL FOR CORNEAL WOUND HEALING
EXTENSIVE PATENT PORTFOLIO COVERING THE APPLICATION
PRODUCT LAUNCH IN 2016
READY TO EXPAND WORLDWIDE

INTELLECTUAL PROPERTY
DEVELOPED BY DR. DAVID KAPLAN, PROFESSOR, BIOMEDICAL ENGINEERING AT LEADING US UNIVERSITY
THE SILK BIO-MATERIAL TECHNOLOGY IS COVERED BY OVER 75 WORLDWIDE PATENTS AND PATENT APPLICATIONS.
TELMA MEDICAL HAS EXCLUSIVE LICENSED RIGHTS TO THE SILK BIOMATERIAL TECHNOLOGY FOR OPHTHALMOLOGY

SILKTEK™ AVAILABLE SIZES
GLAUCOMA PATCH GRAFT:
1.5 x 1.5 CM
Pterygium Graft:
2 x 3 CM
CORNEA SURFACE GRAFT:
9 MM, 12 MM AND 15 MM CIRCLE
Biocompatibility of helicoidal multilamellar arginine–glycine–aspartic acid-functionalized silk biomaterials in a rabbit corneal model

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Tianjin Eye Hospital, Tianjin 300020, China
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May 18, 2017

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Silktek Cornea Lens Pattern
Surface Patterns Control Cell Growth

Silktek® Competitive Matrix For PRK

<table>
<thead>
<tr>
<th>Technology</th>
<th>Strength</th>
<th>Engineered</th>
<th>Cost-Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silktek®</td>
<td>Superior to all Bio Material</td>
<td>Customizable</td>
<td>Cannot cont for rapagl, antiviral, anti-inflammatory agents</td>
</tr>
<tr>
<td>Porokeratosis Human Amniotic Membrane</td>
<td>Arg Strength</td>
<td>Human Biologic</td>
<td>Not Customizable</td>
</tr>
<tr>
<td>Dry Amniotic Membrane Blanks/ Contact lens</td>
<td>Below Avg. Strength</td>
<td>Human Biologic</td>
<td>Not Customizable</td>
</tr>
</tbody>
</table>

Glaucma Treatment Paradigm

Monitoring

Topical therapy

Laser

Cry surgery procedure

Beb

Innovations - Demo Section

Monitoring - H40.1131

- Mild Glaucoma
  - ON
  - Mild concentric narrowing or partial localized narrowing of NRR
  - Disc hemorrhage
  - cup/disc asymmetry
  - NFL
  - Less bright reflex; fine striations to texture; large
  - Retinal blood vessels clear; medium retinal blood
  - vessels less blurred; small retinal blood vessels blurred
  - VF
  - Isolated paracentral scot
  - Omas; partial arcuate or nasal
  - Step; damage limited to one hemifield with fewer than
  - 25% of points involved, mean deviation (MD) less
  - than -6 dB

Monitoring- H40.1132

- Moderate
  - ON
  - Moderate concentric narrowing of the NRR
  - Increase in the area of central disc pallor
  - A complete localized notch or loss of the NRR in one quadrant
  - Undermining of vessels
  - NFL
  - Minimal brightness to reflex; no texture
  - Large, medium, and small retinal blood vessels clear
  - VF
  - Partial or full arcuate scotoma in at least one hemifield
  - Damage may involve both hemifields
  - Fixation should not be involved
  - Mean deviation between -6 and -12 dB
  - Island of vision

Silktek Cornea Lens Pattern
Surface Patterns Control Cell Growth

Silktek Cornea Lens Pattern
Surface Patterns Control Cell Growth
Monitoring –H40.1133

- Severe ON
- Complete absence of the neuroretinal rim in at least three quadrants;
- Bayoneting of vessels
- Markedly increased area of central disc pallor
- NFL
- Reflex dark; no texture;
- Large, medium, and small retinal blood vessels clear
- VF
- Advanced loss in both hemifields;
- 5°-10° central island of vision
- MD worse than -12 dB, fixation may involved

Topical Therapy

- Prostaglandin Analogues
  - Bimatoprost
  - Latanoprost
  - Travoprost
  - Tafluprost

Topical Therapy

- Alpha 2-adrenergic agonists
  - Non-selective
    - Epinephrine
    - Dipiv fen
  - Selective
    - Apraclonidine
    - Brimonidine

Topical Therapy

- Beta Blocking Agents
  - Non-selective
    - Cartelol
    - Levo bunolol
    - Metipranolol
    - Timolol
  - Selective
    - Betaxolol

Topical Therapy

- Carbonic Anhydrase Inhibitors
  - Dorzolomide
  - Brinzolamide

Topical Therapy

- Cholinergic agonists
  - Miotics
    - Pilocarpine soln / gel
    - Carbachol
Topical Therapy
- Combination therapy
  - Timolol-dorzolamide
  - Timolol-brimonidine
  - Brinzolamide-brimonidine

ALT

SLT

Cataract Extraction assoc procedures
- Cyclocryotherapy
- MIGS

Trabeculectomy

Anything else??
- Any other go-tos?
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Issues with Current Paradigm

- Access to care
- Costs
- Compliance
- Side effects of long term treatment

Generics

<table>
<thead>
<tr>
<th>Product</th>
<th>Company</th>
<th>Mechanism</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nepresol</td>
<td>Auven</td>
<td>Inhibition of Rho/kinase and of</td>
<td>Fourth phase 3</td>
</tr>
<tr>
<td>Tefatrasan</td>
<td>Auven</td>
<td>XEPPA and ROCK1 inhibition</td>
<td>phase 1</td>
</tr>
<tr>
<td>Tefatrasan</td>
<td>Auven</td>
<td>XEPPA and ROCK1 inhibition</td>
<td>phase 1</td>
</tr>
<tr>
<td>Valprox</td>
<td>Auven</td>
<td>XEPPA and ROCK1 inhibition</td>
<td>phase 1</td>
</tr>
<tr>
<td>Valprox</td>
<td>Auven</td>
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<td>phase 1</td>
</tr>
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</table>

New Generation Treatments

- Focus on sustained delivery
- Innovative delivery options

Early attempt

- 2008 - anterior juxtascleral delivery of Anecontave acetate – Alcon
- Phase II safety – failed and pulled
- Avg 3.8 mmHg reduction / month

Injectables

- Gray Bug – formed in 2011 as a spin-off of Wilmer Eye Institute carrier molecules

TABLE. GLAUCOMA DRUGS IN THE PHASE 3 PHASELINE

- 2008 - anterior juxtascleral delivery of Anecontave acetate – Alcon
- Phase II safety – failed and pulled
- Avg 3.8 mmHg reduction / month
Gray Bug Injectable

- High drug loading and release of the loaded drug for up to 6 months. → biodegradable polymer matrix (i.e., poly-lactic-co-glycolic-acid, or PLGA)
- Subconjunctival and intravitreal (IVT) injection comparable to approved products administered IVT without inflammation or toxicity through the use of hydrophilic coating and in situ microsphere aggregation to form a depot
- Undisturbed visual axis (no snow globe) post IVT injection due to the localization of microspheres to the periphery of the inferior vitreous.

New Generation Treatments - Injections

Challenges with Current Glaucoma Drugs

- Current approved glaucoma products require daily or thrice-daily dosing
- Patients are non-compliant with therapy (75% in controlled setting, 50% in less controlled practice (Douglas et al.))
- Macrophage agent 10ml/m2 (ciprofloxacin) for long and aggressive (once-weekly, 30%) – dual acting agent (TOP) allows development
- Programs under evaluation ( vidarabine) with 6 month subconjunctival depot formulation
  - Slower drug release, application
  - Single agent UPI (topical) injection
  - Dual agent (des MWU) UPI injection (single packet)
  - IV injection (e.g., IV in conjunctival injection)

New Generation Treatments - Injections

Key Milestones for Value Creation

Sustained reduction of intraocular pressure by supravitreal delivery of intraocular-loaded poly(lactic acid) microspheres for the treatment of glaucoma.

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New Generation Treatments - Implants

- Bimatoprost SR ocular implant
- Allergan

After intracameral injection, the bimatoprost SR "can be visualized in the inferior iridocorneal angle, where it slowly elutes the drug and biodegrades."

In the first 12 weeks, there was a "rapid and sustained" IOP-lowering effect, and a dose response "was generally evident," the authors said. "The magnitude of IOP reduction was typical of a topical ophthalmic prostaglandin."

Mean IOP reduction through week 16 ranged from 7.2 to 9.5 mm Hg. The fellow eye averaged 8.4 mm Hg reduction on once-daily bimatoprost, the authors reported.

Rescue therapy was required in 4 study eyes (5.3%) through week 12 and in 6 study eyes (8%) through week 16.
New Generation Treatments - Implants

<table>
<thead>
<tr>
<th>Ocular Therapeutic</th>
<th>Matt Therapeutic</th>
</tr>
</thead>
<tbody>
<tr>
<td>OTX/TP</td>
<td>L-PPDF</td>
</tr>
<tr>
<td>Travoprost release</td>
<td>Latanoprost release</td>
</tr>
<tr>
<td>Dissolvable intracanalicular</td>
<td>Removable / visible</td>
</tr>
<tr>
<td>Visible via NaFl</td>
<td>Grossly visible</td>
</tr>
<tr>
<td>Phase 2 study</td>
<td>Phase 2 study</td>
</tr>
<tr>
<td>5.6mm implant / 6.7 mm</td>
<td>20% IOP reduction at 12 weeks safety study</td>
</tr>
</tbody>
</table>

New Generation treatments - implants

- The Helios (ForSight Vision5) is a bimatoprost-laden polymer-matrix insert embedded in a compliant ring (Figure).
- Positioned under the upper and lower eyelids visible only at the caruncle.
- Designed to be replaced by a physician every 6 months.

New Generation paradigm

- Advancements in technology
- Hopeful advancement in scope
- What will your new glaucoma paradigm be?

New Generation treatment - implants

- Phase 2 the Helios insert
  - Lowered IOP but less than did topical timolol 0.5% dosed twice daily in eyes with an unmedicated insert
  - Ninety percent of subjects who tried the implant were comfortable, and those who rejected it typically did so within a few days of its placement.
  - A limited sample size of 50 to 60 patients in each arm may have affected the analysis. A much larger phase 3 trial is therefore planned.
OCT Angiography: the Next Chapter in Posterior Imaging

- Images retinal microvasculature without dye injection
- Displays structure and function from a single imaging system

A New Approach to Visualizing Blood Flow

- **Patient Benefits**
  - Reduces patient burden to allow more frequent imaging
  - Avoids potential side-effects of fluorescein injection
- **Clinical Benefits**
  - Faster than a dye-based procedure
  - Ultra-high resolution imaging of retinal microvasculature
  - 3D visualization: segments retinal vasculature into individual layers

Enface OCTA Slabs: Based on Retinal Anatomy

- **Deep Plexus (INL–OPL)**
- **Superficial Plexus (ILM–IPL)**
- **Outer Retinal Zone (ONL–BM)**
- **Choroid Capillaris**

Enface OCTA Overview: Pathology Examples (DR)

- **Superficial**
- **Deep**
- **Outer Retina**
- **Choroid Capillaris**

Enface OCTA Overview: Pathology Examples (CNV)

- **Superficial**
- **Deep**
- **Outer Retina**
- **Choroid Capillaris**

Avascular, Nonperfusion, and Neovascularization

- **Avascular Area**: Significant area devoid of flow signal on an OCT angiogram
  - The foveal avascular zone is a normal avascular area
- **Nonperfusion (Capillary Dropout) Area**: Avascular area that should normally be vascular
- **Neovascularization Area**: Sum of pixel areas in pathologic vessel growth identified on an OCT angiogram
AngioMontage Provides a Wider Field of View

Managing Diabetic Retinopathy

43 Y/O
Type 1 diabetes
A1C 7.4%
FBG 120 mg/dl
Bilateral disc edema 12 years ago – diabetic papillitis
PRP 4 years ago
20/25 OD and OS

Fundus Photos
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Vessel Density Maps Enable Grading of Vascular Change

Ocular Surface Disease/Dry Eye

- Aqueous production
  - True Tear-Allergan
    - Recently FDA approved (April 25, 2017)
    - New development for treatment of ocular surface disease
  - Intranasal Tear Neurostimulator
    - Uses mild electric pulse to stimulate branch of trigeminal V1
    - Research showing stimulates all 3 layers of the tear film
    - Disposable end caps need to be replaced daily
    - Sold by docs and/or Allergan and tips prescribed by optometrist

Ocular Surface Disease/Dry Eye

- Lid treatment/therapy
  - Intense Pulse Light Therapy
    - Flash lamp emits energy from 400 – 1300 nm
      - Filter narrows the range to around 500 nm
      - Hemoglobin absorbs the light energy and eliminates the blood vessels
    - Liquifies "plugged" meibomian gland
  - Introduced in 2002
    - Gaining in popularity

Glaucoma

- ROCK-NET Inhibitors
  - Rho kinase inhibitor
    - Relaxes TM cell
  - Lower episcleral venous pressure
  - Norepinephrine inhibitor
    - Reduces fluid production
    - Ciliary body and other structures
  - New class of IOP lowering medications

- Rhopressa 0.02%
  - ROCK-NET inhibitor
- Roclatan
  - ROCK-NET Inhibitor and latanoprost

What’s Potentially Coming

- Valeant Pharmaceuticals International has rebranded Vesneo as Vyzulta

- Vyzulta-latanoprostene bunod ophthalmic solution 0.024%
  - Nitric oxide-donating prostaglandin F2-alpha analog
  - Intended to treat patients with glaucoma or ocular hypertension

What’s Potentially Coming
What’s Potentially Coming

- **Trabodenoson**
  - Inotek Pharmaceutical
  - Compound is considered to be a first-in-class selective adenosine mimetic
  - Action appears to be increased trabecular aqueous outflow
- **Stimulates adenosine receptors**
  - Increasing metabolic activity in the trabecular meshwork
  - The increased metabolic activity up-regulates proteases that digest and remove accumulated proteins which hinder trabecular aqueous outflow

MIGS

- **Minimally Invasive Glaucoma Surgery**
- More than
  - iStent
  - ECP- Endoscopic Cyclo-Photocoagulation

Minimally Invasive Glaucoma Surgery (MIGS)

- Schlemm’s Canal/Conventional outflow
  - iStent
  - iStent inject
  - Hydrus
  - Trabectome
  - Dual Blade
  - GATT 360
  - Trab 360/Visco 360
- Suprachoroidal Space
  - Cypass
    - iStent Supra
  - Scleral/Subconjunctival
  - Xen

Cypass

- Suprachoroidal Space
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Xen

- Scleral/Subconjunctival
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Xen Scleral/Subconjunctival

Refractive IOLs

Acrysof IQ ReSTOR Toric Multifocal Intraocular Lens (Alcon)

Technis Symfony Toric MF

Questions
Thank You!