INNOVATIONS IN EYE CARE

Clinical Director, Corneal Services and OSD Center
Kentucky Eye Institute, Lexington KY
Gaddie Eye Centers, Louisville KY
Financial Disclosures:

AcuFocus
Aerie Pharmaceuticals
AMO
Alcon Labs
Allergan Inc
Akorn
Anthem
Arctic Dx
Bausch & Lomb Inc
Beaver Visitech
BioTissue
Bright Optical
Bruder Healthcare
Cambium Pharma
Candor Pharma
Enchroma
Essilor
EyeMaginations
Eyes4Lives
EyeSolutions
Focus Laboratories
Freedom Meditech
Glaukos
iCare USA
Imprimis
J&J
Katena
Konan Medical
Ocular Dynamics
Oculus
Ocusoft
Ocular Therapeutix
Optometric Medical Solutions
Paragon Bioteck
PECAA
Perrigo
Reichert
Regeneron
RySurg
Science Based Health
Sensor Medical
Sentiss Pharma
Shire Pharmaceuticals
Sight Risk
Smart Vision Labs
Sun Pharmaceuticals
TearLab
TearScience
Tearfilm Innovations
TelScreen
TLC Vision
Topcon
VisionMetrics
Vision Care Inc
Vmax
Vollya
Stem Cell Technologies
Limbal Stem Cell Deficiency

Sequele

- Persistent epithelial defects
- Corneal scarring and ulceration
- Conjunctivalization of the cornea
- Severe visual loss
- Chronic pain
- Keratoplasty failure
Limbal Stem Cell Transplantation

**Procedures**

**Autograft**
- Conjunctival limbal autograft  
  *fellow eye*

**Allograft**
- Living-related conjunctival limbal allograft  
  *relative*
- Keratolimbal allograft  
  *cadaver*
Keratolimbal Allograft

Donor

Recipient

Patient's limbus

Donor limbus
RPE Tissue regenerated from Stem Cells
RPE Tissue Regenerated from Pluripotent Skin Stem Cells
Stem Cell Coated Contact Lenses

- Aniridia patients
- Contact lens overwear?
- Various ocular surface disease issues:
  - Steven’s Johnson syndrome
  - Ocular pemphigoid
  - GVH
  - Chemical burns
Sensimed Triggerfish lens: Diurnal IOP measurements
Glucose Monitoring Contact Lens
PROKERA®

- Class II medical device comprising of CRYOTEK™ amniotic membrane into a thermoplastic ring set
- Combines the functionality of a symblepharon ring with the biologic actions of CRYOTEK™ amniotic membrane to create a unique treatment option for corneal and limbal wound healing
Clinical Evidence for PROKERA®

- A safe and effective method to promote healing of the corneal surface with minimal side effects\(^1\)
- Inhibits abnormal angiogenic processes and inflammation, thus promoting scarless healing\(^1-7\)
- Stimulates healthy re-epithelialization of the corneal wound without sutures\(^1,2,4-6,8\)
- Provides pain relief and reduces haze, resulting in improved visual acuity by a mean (SD) of 2.5 (2.6) Snellen lines\(^2\)

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outer Ring Diameter:</strong></td>
<td>21.6 mm</td>
<td>21.6 mm</td>
<td>21.6 mm</td>
</tr>
<tr>
<td><strong>Inner Ring Diameter:</strong></td>
<td>17.9 mm</td>
<td>15.5 mm</td>
<td>15.5 mm</td>
</tr>
<tr>
<td><strong>Device Height</strong></td>
<td>0.7 mm</td>
<td>1.1 mm</td>
<td>1.1 mm</td>
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<tr>
<td><strong>Tissue Thickness</strong></td>
<td>Single Layer</td>
<td>Single Layer</td>
<td>Multiple Layers</td>
</tr>
<tr>
<td><strong>Ring Description</strong></td>
<td>Ring &amp; Elastomeric Band System (polycarbonate)</td>
<td>Dual Ring System (polycarbonate)</td>
<td>Dual Ring System (polycarbonate)</td>
</tr>
</tbody>
</table>
PROKERA® Insertion & removal

• Set patient expectations! Inform the patient they may experience some initial stinging and foreign body sensation
• Apply topical anesthesia
• **Rinse** the PROKERA® with a sterile solution (saline, BSS etc...)
• Hold the upper eyelid
• Ask the patient to look down
• Insert the PROKERA® into the superior fornix, preferably using your fingers to hold the ring
• Slide the PROKERA® under the lower eyelid
Amniotic Membrane Treatment

Spina Bifida
Point-of-Care Diagnostics
Adeno Plus Detector™

Reading & Interpreting the Results

Positive Results:

The **Results Line and Control Line** are **RED** in the result window, indicating that Adenovirus antigen **is present**.
INFLAMMADRY™

Reading & Interpreting the Results

Positive Results:
Means MMP-9 greater than 40 units per sample
TearLab
# Osmolarity in the Diagnosis of Dry Eye Disease

<table>
<thead>
<tr>
<th>Clinical Test</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolarity</td>
<td>87%</td>
</tr>
<tr>
<td>Schirmers</td>
<td>31%</td>
</tr>
<tr>
<td>TBUT</td>
<td>25%</td>
</tr>
<tr>
<td>Staining</td>
<td>31%</td>
</tr>
<tr>
<td>Meniscus Height</td>
<td>33%</td>
</tr>
</tbody>
</table>

Source: DEWS Report, Ocular Surface April 2007 Vol 5 No 2, & Tomlinson A, et. al., IOVS 47(10) 2006
TearLab™ Precision @ 50 nL

- < 2% coefficient of variation @ 50 nanoliters
  - Glucose $\geq 5.0\%$ CV @ 5 microliters
  - Cholesterol $> 4.0\%$ CV @ 20 microliters

- Safe, simple collection
  - No reports of corneal or conjunctival trauma in 468 eyes [TearLab™ FDA 510(k) submission]

- Winner 2009 MDEA for In Vitro Diagnostics

Osmolarity in Diagnosis & Grading of Dry Eye

- Normal
- Mild
- Moderate
- Severe

Osmolarity (mOsm/L):
- 275
- 290
- 305
- 320
- 335
- 350
- 365
- 380
- 400

Variability (σ) mOsm/L:
- < 5 mOsm/L
- ≥ 20 mOsm/L
Tear Film Instability Increases With DED Severity

Mathematical model derived from Fig. 3:
Future of Tear Biomarker Analysis:

TearLab Next Generation Platform

• Quantitative
• Ability to measure
  – Osmolarity
  – Inflammation biomarkers
  – Allergy biomarkers
  – Specific drug related biomarkers
• Rapid testing (< 2 minutes)
• Multiplexed biomarkers
• EHR Integration
• Clinical Application:
  – Normalization using osmolarity
  – Customized chips with designed sensitivity & specificity
TearLab Next Generation Platform

• When?
  – CE Mark by end of 2016
  – 510k submission in early 2017
    • First test will have osmolarity + 1 or 2 additional markers
    • Likely to be focused on inflammation
    • New iterations possible every 6 months
TelScreen
TelScreen
Meibography
Annidis RHA Imaging
PARTIAL OR INFREQUENT BLINKING
LipiFlow® Thermal Pulsation

LipiFlow® is the only FDA-cleared device for Meibomian Gland Dysfunction (MGD), shown to restore gland function.

LipiFlow® is an in-office procedure, taking 12 minutes per eye.
Core Therapy: Treat obstruction

Novel Approach:
Heat the inner lid surface with simultaneous gland evacuation

Safe, effective, precise, proven:
• Restores Meibomian Gland function
• Applies a combination of heat and pressure directly to the inner eyelid
• FDA-cleared and clinically approved
• Independent proven results in peer-reviewed studies
1,2,3

1. Finis, D. et al. Ocular Surface 2014 Apr; 12(2); 146-54
Bruder Eye Hydrating Compress

- Moist heat compress
- 30 angstrom opening pulls in ambient hydration and then release
- 20-25 seconds in microwave
- Brings MG temperature over 104 degrees for ~10 min
- Antibacterial via silver ionization
- Washable, durable
BlephEx
BlephEx & BioFilm Treatment
Oculeve Technology

- Tear stimulant for aqueous deficient dry eye
- Inserted in nasal canal
- Wireless stimuli to create tears
EyeGraine: Subgroup of Chronic Daily Headache

 Symptoms

- Primary Symptoms
  - Frequent Headaches
    - 3+ days per week
  - Neck Pain/Stiffness

- Secondary Symptoms
  - Dry eyes
  - Fatigue with near work
  - Photophobia, especially at night
    - headlights
Study Data

- Unchanged: 6.74%
- Decreased Slightly: 25.84%
- Decreased Substantially: 53.93%
- Basically Gone: 13.48%

Total: 67%
70% off of at least some medications at 90 days

52% of patients off of 50% or more of their headache medications

No reported side effects
Research confirmed

- Pursuits and Saccadic eye movements
  - Sends it proprioceptive signal via the trigeminal nerve
    - Ophthalmic branch
- Trigeminal Nerve (V):
  - Stimulation of Ophthalmic branch
    - Frontal headaches (sinus headaches)
    - Terminates in lower brain stem (back of head headaches /neck pain)
    - Cornea sensation (Dry Eye)
neuroLens™

Reading Zone

Base in prism
Based on your experience in the first 90 days of the eyeGraine Treatment Plan, would you be willing to recommend eyeBrain Medical to your friends and family?

Answered: 89  Skipped: 0

Yes: 96.63%
No: 3.37%

n = 89  50
Collagen Cross Linking (CXL)
Ectasia Diagnosis and Management
Corneal Cross-Linking

- First introduced by Theo Seiler MD
- Involves saturating the cornea with riboflavin (Vit B2)
- Expose cornea to UV light (370 nm) for 30 minutes
- Riboflavin absorbs UV light and produces singlet oxygen
- Causes cross-linking of collagen fibers and extracellular matrix proteins
- To protect the endothelium:
  - Soak cornea for 30 minutes prior
  - Originally required debridement of corneal epithelium
  - Ensure riboflavin has penetrated to the AC
Corneal Cross-Linking

- Riboflavin prevents penetration of uv light
- Older corneas vs. younger corneas and progression of keratoconus
- CXL appears to be the first technology than can halt the progression of ectasia
Other potential applications

• Physician sponsored IND for infectious keratitis treatment
  – Ulcers limited to 250 microns
  – May also help with infectious load

• Treatment of corneal edema
  – Cross linking reduces imbibition pressure
  – Internationally it appears to work for 3 mo to 12 mo duration

• Treatment for fluctuating vision post RK
DALK-Deep Anterior Lamellar Keratoplasty

lamellar keratoplasty

image courtesy of Dr. L. Buratto
Presbyopia Correction

- Accommodating IOLs
- Corneal Inlay Technology
AcuFocus KAMRA Inlay
Inlay Design

Total diameter: 3.8mm

Aperture: 1.6mm

Thickness: 5 μm
Surgical Procedure

- Description: A femtosecond laser created pocket in the stroma at a depth of 200-250μm with femtosecond laser spot/line settings of < 6x6 or equivalent is recommended.

Pocket Emmetropic KAMRA (PEK)
KAMRA Inlay Design

- Inlay improves near vision by extending depth-of-focus
- Central aperture is a hole in the inlay and has no power
- Inlay provides an unobstructed pathway for focused light to reach the retina
Depth of Focus Pre-Op & Post-Op

Pre-op

0.25D of depth of focus

Several Months Post-op

2.50D of depth of focus

OQAS Accommodative Range (D): 0.25

OQAS Accommodative Range (D): >2.50

AcuTarget HD™ Instrument
Clinical Study Outcomes

» Change between Pre-Op and 36 Months:
  » Mean UCNVA improved 5 lines from J8 to J2
  » Mean UCDVA reduction from 20/18.5 to 20/20
  » Mean MRSE changed from 0.02 + 0.28 D to 0.14 + 0.72 D

<table>
<thead>
<tr>
<th></th>
<th>Pre-Op</th>
<th>36 Months</th>
<th>&gt; J5</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCNVA</td>
<td>13%</td>
<td>53%</td>
<td>91%</td>
</tr>
<tr>
<td>UCDVA</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

*N=153 at 36 months, ≤ 6x6 group, data on file at AcuFocus™
RainDrop

- Phase III clinical trials
- Hydrogel Inlay
- Increases prolate nature of cornea
- Under a femtosecond flap
Refocus

- Restarted Clinical trial with redesign of method for creating the tunnels
- Now called the “visibility implant system”
Calhoun Light Adjustable IOL

- Currently available in Europe
- 6 mm silicone optic and PMMA haptic IOL
- Using a UV laser so as to change the refractive error
- Post operative enhancement, correction, adjustment
- Optometry’s role in 8-10 years
Calhoun Light Adjustable IOL

- Optometry role
- UV light adjustable
- Working on payment system currently
Topical ‘CURE” for Presbyopia

• Eye Therapies
  • Contains miotics but also proprietary components that allow full 12-14 hours of near and far vision

• Encore Vision
  • Contains drops that selectively target and disrupt the disulfide bonds in the lens
  • Total of 3-4 weeks of treatment and permanent results thus far
Higher proportion of EV06 subjects had gain of 10 letters or more (DCNVA) compared to placebo.

Note: Preliminary analysis based on LOCF in study eye only.

Percent of Subjects with Gain of ≥10 Letters in DCNVA

Day 8  Day 15  Day 31  Day 61  Day 91

Placebo  EV06

P=0.003  P=0.04

P-value is based on Fisher’s exact test.

DCNVA=Distance-corrected near visual acuity

Note: Preliminary analysis based on LOCF in study eye only.
How Is Accommodation Lost?
Why Does Presbyopia Happen?

Young Eye

Cytosol Displacement Centrally = Accommodation

Aging Eye

Oxidation induced disulfide bonds form between crystalline proteins - a Leading Potential Cause

Lens Stiffening = Compromised Accommodation
What is EV06?

How Does it Work?

- EV06 (Lipoic Acid Choline Ester, 1.5%) is a **prodrug**

- EV06 penetrates cornea - metabolized into **Choline & Lipoic Acid**, two naturally occurring substances

- Enzymes within lens fiber cells chemically reduce **Lipoic Acid** to active form **Dihydrolipoic Acid**
LENS ELASTICITY IS REGAINED

Dihydrorlsopic Acid

Dihydrolipoic Acid Chemically Reduces Disulfide Bonds

Cytosol Displacement Centrally = Accommodation
EV06 Safety & Tolerance Results

• No Subjects Discontinued For Adverse Events, Safety Concerns, or Tolerability

• No Sight Related Adverse Events

• Upon Instillation
  – Mean EV06 Comfort Rating 3.0
  – Mean Placebo Comfort Rating 2.7
    • (Scale 0 – 10; “0” = Very Comfortable)

• No Change In Best Corrected Distance Visual Acuity
EV06 Efficacy Results

- Achieved both Primary Efficacy Results:
  - Improvement in Distance Corrected Near Vision Acuity (DCNVA) in the Study Eye after treatment, which continued throughout the dosing period
  - Higher proportion of subjects with gain of ≥10 letters in DCNVA in the study eye vs. placebo
**Improvement in Distance Corrected Near Vision Acuity**

**DCNVA LogMAR - OU**

- **LogMAR Score**
- **Treatment Day**

Graph showing the improvement in Distance Corrected Near Vision Acuity (DCNVA) over treatment days. The graph compares Placebo (green line) and EV06 (blue line) treatments. Key p-values for the two-sample t-test (EV06 vs. Placebo) are:
  - P=0.017
  - P=0.022
  - P=0.027
  - P=0.005

**P-values** indicate statistical significance in the improvement of vision acuity between the two treatments.
Percent of Subjects with Gain of ≥10 Letters in DCNVA

Note: Preliminary analysis based on LOCF in study eye only
EV06 DCNVA Snellen score - Day 1 & Day 91

- Improved shift in Snellen Scores
Placebo DCNVA Snellen score - Day 1 & Day 91

- No material shift in Snellen Scores
Implant Technologies
ARGUS II

- Inserted onto macula
- Contains a circuit board that allows for 32,000 pixel images
- Stimulates via a wireless system to provide electrical current to occipital lobe
- Uses glasses as transducer
- Allows for image of shapes or shadows
- $100,000 to patient
- Future expectations for over 100,000 pixels
Implantable Miniature Telescopes

- Renders retinal image ~2.7x larger than natural lens
  - Images seen upon viable perimacular tissue
  - Field of view 20-24 degrees
- 67% achieve >/= 3 lines of improved VA (control = 13% - worse seeing eye for treatment eye)*
- Improved ADL’s and Vision-Targeted Psychosocial Domains*

Glaukos iStent

*iStent is the smallest medical device known to be implanted in the human body and weighs just 60 µg*
Glaukos iStent

*iStent® is designed to be used in conjunction with cataract surgery to safely and effectively reduce IOP while facilitating the eye’s natural outflow in mild to moderate OAG patients currently on hypotensive medication

- Lowers IOP and may reduce or eliminate medication burden\(^1\)
- Decrease risk of IOP fluctuations associated with non-adherence to prescription medication regimens
- Avoid serious complications associated with end-stage filtration and shunt procedures
- Spare the conjunctiva and safely preserve future treatment options
- Minimizes risks of hypotony and bleb related complications
Gene Therapy & Genomics

• Generic variants causing most ocular diseases are being discovered
• Examples include glaucoma, dry AMD, Fuchs’ and all corneal dystrophies
• Early treatment vs. repair
• Focusing on rare diseases such as RP currently
• Ocular anatomy and architecture are uniquely situated for gene based research
First degree relatives of people affected by AMD are at significantly increased risk of AMD.
Clinical Assessments – 1446 Patients (AREDS 1)

“Clearly, genetic factors play a major role…”

“The predictive power of this composite of risk factors for progression to advanced AMD, with a C statistic score of 0.83, is comparable to the Framingham risk functions for CHD in which the C statistics were 0.79 for white men and 0.83 for white women”

2009 - Validated combination of CFH, C3, ARMS2
2012 - more genes + Drusen size – 0.91 ‘C’ statistic score

AMD – A Genetic Disease

Macula Risk

A test that identifies AMD patients who will progress to vision loss

Cheek Swab
Macula Risk Score

Risk of Progression from early / intermediate AMD to advanced AMD with vision loss

- Average Population
  - 50%
  - 30%
  - 16.8%
  - 2.2%
  - 1%

Macula Risk 3, 4 & 5 = 20% of the Caucasian population
Genetic Specificity

- 49% of patients derive more benefit from a formulation other than AREDS.
- For 23% of patients, the AREDS formulation was the best treatment.
Medical Utility - The AMD Problem

Only 15% to 20% of Early / Intermediate AMD will progress to Advanced disease

How can the Primary Eye Care Professional identify those at Risk?
AdaptDx

Photoreceptors

Sclera

Cholesterol accumulation leads to panmacular deposits (BlinD and BlamD)

Peaks in these deposits eventually become clinically visible drusen

These extracellular cholesterol deposits affect photoreceptor health by impairing transport, causing inflammation, and predisposing to CNV

In addition, they impair normal transport, including that of vitamin A, across Bruch’s membrane

Dark adaptation is the process of adjusting from day vision to night vision

Easy-to-measure aspect of night vision
AdaptDx

First dark adaptometer for rapid, routine clinical use

Simple, objective tool to measure dark adaptation as earliest functional correlate of macular dystrophies

Two clinical protocols
- ≤6.5-minute rapid test (for quick assessment)
- ≤20-minute extended test (for benchmarking)
Crizal® prevencia™: blue-violet light protection

- Protection from Blue-Violet light
- New No-Glare lens treatment
- Features Light Scan™
- Selectively deflects harmful Blue-Violet light by 20%
- In recent lab tests, Crizal Prevencia lenses reduced retinal cell death by 25%*
- No other No-Glare lens on the market offers selective protection against harmful Blue-Violet light
BluTech Lenses

Filter Blue Light
Block UV
Available as Indoor or Outdoor (Polarized Sunglass) Lenses
Plano, Finished RX Indoor, Single Vision, Flat-Top 28 and Progressive Designs
• VSP UNITY PLx, Plxtra, CVx
• Shamir Autograph I,II,III + Shamir Computer & Workspace
• All Kodak Back Surface Progressives (Unique/Precise PB/PB Short)
• Hoya ARRAY Progressive
• Select Private Label Progressives (IOT)
Lens, NOT a Coating
Lens Monomer infused with Ocular Lens Pigment and Melanin Pigment
Who needs most protection?

- HIGH Exposure to White LED or Fluorescent Light Bulbs in offices/homes
- Frequent user of LED computer monitor, Tablet and Smart Phone
- At-risk of AMD or other Pathologies, Kids or Drugs
Robotics in Ophthalmic Surgery
Robotics in Surgery

- da Vinci is the first surgical system approved by the U.S. FDA for minimally invasive general surgery in 2000
- Increasingly becoming standard equipment in many operating rooms
- Temple University presented the potential use of the da Vinci robot in transscleral, subretinal injections
- No tremor, reduction in incidence of RD
Topical Wet AMD Treatment?

- OHR-102 Phase II IMPACT Study in Wet AMD Shows Positive Results
- 0.2% Squalamine lactate ophthalmic solution combination therapy for the treatment of wet AMD
- Data presented included the analysis of visual acuity outcomes for patients completing the nine-month treatment period
Topical Wet AMD Treatment?

- mITT population with lesions containing classic choroidal neovascularization (OHR-102 n=37, Lucentis monotherapy n=28), mean gains in visual acuity at month nine were +11 letters vs. +five letters with Lucentis

- 44% of the patients achieved $\geq 3$ line vision gain at nine months (as compared to 29% in the Lucentis monotherapy group)
Ocular Therapeutix Drug Deliver

- Dextenza post cataract
- Dextenza for allergic conjunctivitis*
- Sustained release Travoprost
- Dry eye therapy via a punctal plug
Absence of Ocular Pain

- OTX-DP (N=29)
- PVPP (N=30)

Days:
- 1
- 4
- 8
- 11
- 14
- 30

Patients (Pain=0):
- 0%
- 20%
- 40%
- 60%
- 80%
- 100%
Imprimis DropLess and Less Drops
**Delivery Technique**

Surgeons currently using our formulations believe the optimal location for the injection would be the vitreous due to the depot effect.

This is achieved by one of two approaches:

1. *Pars plana injection via needle*
2. *Transzonular injection via cannula*

Typical dose administered = ~0.2 cc
Color Deficiency

- Affects 1 in 200 females
- Affects 1 in 8 males
- 30 Million Americans have some level of color deficiency
- Deuteranopia being most common
- Protanopia occurs more often with acquired disease
- Ishihara misses 100% of protanopia
ColorDx Expanded

Validated by Naval Aerospace Medical Institute

Used to qualify military aviators
Recommended for approval for the FAA
Multi-Format

Android tablet app
Windows app
(including CellChek + Chart2020)
iOS app (Q2 2014)
Precision-print booklets
Enterprise - Web
Color Deficiency
Enchroma

Super-Hydrophobic Coating
Anti-Reflection Coating
Scratch-Resistant Hard-Coating

EnChroma Cx
Spectral Multi-Notch Filter

Polycarbonate Lens
Refractive index: 1.59

Scratch-Resistant Hard-Coating
Backside Anti-Reflection Coating
Super-Hydrophobic Coating
New Medications
Lifitegrast (Shire Pharmaceuticals)

- Lifitegrast is a novel LFA-1 antagonist that targets chronic inflammation in dry eye disease (DED)
- In an earlier Phase 3 trial (OPUS-1), lifitegrast met the coprimary efficacy endpoint of change in inferior corneal staining score, a sign of DED, from baseline to day 84¹
- OPUS-2 met prespecified primary symptom of ocular dryness
- SONATA was a 1 year safety trial
- OPUS-3 met prespecified primary symptom of ocular dryness

Results: Coprimary Endpoints

Symptom:
Eye Dryness (VAS; 0-100)
\( P < 0.0001 \)

Sign:
Inferior Corneal Staining (0-4)
\( P = 0.6186 \)

Figures show observed data and endpoint with LOCF. \( P \) values above figures refer to endpoint with LOCF. SE, standard error.
Results: Primary Endpoint (ITT Population with LOCF)

**Eye Dryness Score**

VAS, 0–100 points (0=no symptoms, both eyes)

Change from baseline to Day 84
-37.9 lifitegrast versus -30.7 placebo

TE, 7.16; 95% CI, 3.04 to 11.28; \( P=0.0007 \)

CI, confidence interval; ITT, intent-to-treat; LOCF, last observation carried forward; SE, standard error; TE, treatment effect; VAS, visual analogue scale.
**Results: Key Secondary Endpoints (ITT Population with LOCF)**

**Eye Dryness Score**

VAS, 0–100 points (0=no symptoms, both eyes)

- **Change from baseline to Day 14**
  - -22.9 lifitegrast versus -15.0 placebo
  - TE, 7.85; 95% CI, 4.33 to 11.37; \( P<0.0001 \)

- **Change from baseline to Day 42**
  - -33.2 lifitegrast versus -23.9 placebo
  - TE, 9.32; 95% CI, 5.44 to 13.20; \( P<0.0001 \)

CI, confidence interval; ITT, intent-to-treat; LOCF, last observation carried forward; SE, standard error; TE, treatment effect; VAS, visual analogue scale.
OPUS-2 and OPUS-3

Eye Dryness Score
VAS, 0–100 points (0=no symptoms, both eyes)

**OPUS-2**
(ITT Population with LOCF)
TE (baseline to Day 84): 12.61; 95% CI, 8.51 to 16.70; \( P<0.0001 \)

**OPUS-3**
(ITT Population with LOCF)
TE (baseline to Day 84): 7.16; 95% CI, 3.04 to 11.28; \( P=0.0007 \)

* \( P<0.0001 \); CI, confidence interval; ITT, intent-to-treat; LOCF, last observation carried forward; SE, standard error; TE, treatment effect; VAS, visual analogue scale.
Treatment-Emergent Adverse Events (TEAEs)

- Lifitegrast was generally well-tolerated in this study
- No serious ocular TEAEs were observed
- Most ocular and non-ocular TEAEs were mild in severity

<table>
<thead>
<tr>
<th>Most frequent (&gt;5%) TEAEs, n (%)</th>
<th>Placebo (n=354)</th>
<th>Lifitegrast (n=357)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instillation site irritation</td>
<td>11 (3.1)</td>
<td>65 (18.2)</td>
</tr>
<tr>
<td>Instillation site reaction</td>
<td>19 (5.4)</td>
<td>45 (12.6)</td>
</tr>
<tr>
<td>Dysgeusia (change in taste)</td>
<td>1 (0.3)</td>
<td>46 (12.9)</td>
</tr>
</tbody>
</table>

- Discontinuations due to TEAEs were infrequent (lifitegrast, 5.9% [21/357]; placebo, 2.5% [9/354])
  - The most common TEAEs that led to discontinuation were instillation site reaction (lifitegrast, n=5; placebo, n=2) and instillation site irritation (lifitegrast, n=4; placebo, n=0)
Other Safety Findings

• Drop comfort (DC) score* with lifitegrast improved within 3 mins of instillation and showed consistent reductions across visits
  • Mean DC with lifitegrast at instillation improved across visits (lifitegrast vs. placebo: baseline, 4.4 vs. 1.2; Day 84, 3.4 vs. 1.0)
  • The majority (64–66%) of subjects receiving lifitegrast reported DC <3 at 3 mins post instillation

• Signs were also measured as part of the safety assessment
  – Corneal fluorescein staining score, conjunctival lissamine green staining, conjunctival redness score, and Schirmer Tear Test demonstrated greater numerical improvement over time in the lifitegrast versus placebo groups
  – Best Corrected Visual Acuity, slit lamp biomicroscopy, and dilated fundoscopy were comparable between treatment groups

*Drop comfort score using 0–10 point scale (0=very comfortable, 10=very uncomfortable).
Dry Eye Pipeline

- Lifitigrast (Shire)
- Mimetogen (Allergan)
- RU-101
- Rebamipide (Otsuka)
- KPI-121
- Kala (cyclosporine)
Lifitigrast (5.0%)

- Significantly improved the coprimary symptom of eye dryness compared with placebo
  - Symptom improvements were observed as early as day 14 with maintenance of benefit through day 84
  - Improvements were observed in secondary and tertiary VAS endpoints in support of the coprimary endpoint
- Results for symptom improvement in this trial are notable in the context of previous studies in DED
Rebamipide 2% (Otsuka)

- Topical Mucin secretagogue
- Designed to stimulate increased mucus in the cornea and conjunctiva
- Phase II shows statistical improvement in signs and symptoms for dry eye patients
- Currently in phase III
RU-101 (R-Tech Ueno)

• Recombinant human serum albumin
• One of the key proteins found in autologous serum
• Phase II trials currently
KPI-121 (Kala Pharma)

- Topical Mucin secretagogue
- MGD target in clinical trials
- Loteprednol etabonate mucus-penetrating particle (MPP)

- B+L also has a nano particle LE in development
Anti-viral

Foresight Biotherapeutics FST-100

- Anti-viral
- Involves povidone iodine + dexamethasone
- Povidone iodine is used as an anesthetic perioroperatively now and even for EKC
- Often significant inflammation associated with it and hence the dexamethasone
Glaucoma Medications

- B+L Licensed
- Nitros oxide sparing prostaglandin analogue
- Lowered IOP by 9.1mm compared to 7.3 for timolol arm in phase III trial
Glaucoma Medications: Rho Kinase (ROCK) Inhibitors

- Works on TM
- Acts like a muscle and may decrease tension
- Two products in development
  - AMA0076, Amakem Therapeutics
  - Rhopressa (AR12286), Aerie Pharmaceuticals
Glaucoma Medications: Rho Kinase (ROCK) Inhibitors

• Aerie Pharmaceuticals
  • Triple-action Rhopressa™
    • Targets the TM
    • Lowers scleral venous pressure as well
    • Phase III started in July 2014 and accelerated reporting
  • Quadruple-action Roclatan™
    • Rhopressa™ + latanoprost
    • Phase IIb
Glaucoma Medications: Lim (ROCK) Inhibitors

- LM7101, a Lim kinase 2 inhibitor
- Lexicon Pharmaceuticals
- New class of treatment
Baseline IOP < 24 mmHg (Prespecified analysis)

- AR-13324 was non-inferior to timolol in this subgroup
Baseline IOP < 25 mmHg At All Time Points

- AR-13324 was non-inferior to timolol in this subgroup
Quadruple-Action PG324 (ROCK-NET Inhibitor/latanoprost)

Fixed Combination of AR-13324 with Latanoprost

4 Identified IOP-Lowering Mechanisms

- ROCK inhibition relaxes TM\(^1\), increases outflow\(^{1,2}\)
- NET inhibition reduces fluid production\(^2\)
- ROCK inhibition lowers EVP\(^3\)
- PGA receptor activation increases uveoscleral outflow\(^4\)

4. Latanoprost prescribing information
PG324 Achieved Statistical Superiority Over Individual Components at All Time Points (p<0.001)

Mean IOP at Each Time Point (Primary Efficacy Measure)

PG324 Phase 2b, Intent to Treat
PG324
Phase 2b Responder Analysis

Day 29 – % of Subjects with IOP Reduced to ≤ 18 mmHg

Glaucoma Medications: Adenosine Receptor Agonists

- INO-8875 (Inotek)
- Adenosine R1 agonist
- Works by enhancing outflow by stimulating the secretion of matrix metalloproteinases
- Results in TM tissue remodeling
Glaucoma Medications: Adenosine A3 Receptor Agonists

- ACN-1052 (Acorn Biomedical) and CF-101 (Can-Fite BioPharma)
- Oral medications
- Reduce IOP by inhibiting aqueous humor production of the ciliary epithelium via blocking signaling pathway
Glaucoma Medications: Neuroprotection

- Ophthalix CF101
- A3 adenosine receptor agonist
- Inhibits neutrophil degranulation and may have neuro-protective effects
- Oral medication
- Also being studied for uveitis and glaucoma
CF101

- Oral administration
- Adenosine is a neurotransmitter
- Has been shown to have an affect on the CNS but acts peripherally
- **Inhibits leukotriene B4** which is part of the arachidonic acid pathway
Retina: Wet AMD, CME, DME

- Anti-VEGF: Macugen, Lucentis, Avastin, Eylea
- Steroid: Retisert, Osurdex & Iluvien
- Eylea (anti-VEGF)
  - most recent approval
  - longer duration, better binding properties, dries better
Retina: Wet AMD, CME, DME

• Future:

• Conbercept (Chaengdu Kanghong Biotech)
• PDGF - Platelet derived growth factor (Regneron)
  • Affect pericytes on the newly formed BV’s that make them more susceptible to anti-VEGF treatment
Uveitis

• Future:
  • Sarilumab (Regeneron)
    • Anti-inflammatory 6 (IL-6)
    • Originally planned for RA but shown to have non-infectious uveitis treatment potential
Eye Whitening

Luminesse (B+L)
- Eye whitener
- Low dose alpha adrenergic
- 300% whiter eyes than Visine
- Lasts 4-8 hours
- No rebound hyperemia
The importance of good communication...
THANK YOU!

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