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- More than 50% of exercise regularly
- 72% of boomers plan to keep working in some capacity after retirement
- 83% of Boomers are on the internet and spend more hours per week on computer than TV
- 72% of Boomers have a cell phone and check it on average 46 times per day!

Data on file, Bausch & Lomb Incorporate Hardy. Love to Know website. 2012. Del Webb 2010 Baby Boomer Servey Sauer et al. Defoitte Research. 2012. Jones. Pew Research Center. 2009.











Helmholtz, 1855



#### **Binocular Vision Issues**

- Consider:
- The convergent insufficient who can no longer accommodate to accommodate
- The post-LASIK "former" myope with symptoms of asthenopia
- Accommodative insufficient



# The Aging Lens

The adult lens contains the embryonic nucleus

The embryonic nucleus contains the oldest cells and proteins in the lens

The embryonic nucleus is surrounded by the fetal nucleus, the juvenile nucleus and the adult nucleus

The nucleus is surrounded by the cells of the cortex which are the youngest cells in the lens

Kuszak, J.R., AL-Ghoul, K.J. and Costello, M.J. Duane's Clinical Ophthalmology, 2006.

Summer and a summer

cap

# Aging of Lens Crystallins

Crystallins are normally water soluble lens proteins

With age they undergo post-translational modifications including racemization, deamidation, oxidation of amino acid sub-groups

This results in degradation, backbone cleavage...

... which alters the protein three dimensional structure,...

... allows inter-molecular disulfide bonding,...

... exposes the hydrophobic core...

... and leads to aggregation, insolubility, lens stiffening and cataract

Hanson, S. R., Hasan, A., Smith, D. L. & Smith, J. B. Exp. Eye Res. 2000, 71, 195-207.











# Contact Lenses Multifocals Monovision Modified Monovision Various designs/modalities What's the appropriate expectation? Suppopriate expectation?

























# **Light Treatments**

Light Treatments are Painless, Non-Invasive and Last Approximately 90 Seconds



 
 Light Treatment Schedule

 Initial Light Treatment
 At Least 17 Days After Surgary

 Secondary Light Treatment
 At Least 3 Days After Initial Light Treatment

 Additional Light (#reatments)
 At Least 3 Days After Each Prior Light Treatment



# Pupil Modulation Contains miotics but also proprietary components that allow for near and far vision Lens softening Contains drops that selectively target and disrupt the disulfide bonds in the lens









# 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

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# Emerging Treatments—Miotics

#### MOA: Decrease pupil size

 Increases DoF and clears image by limiting entering light to central parallel rays that converge at a focal point on the retina

#### AGN-190584

- Two 30-day vehicle-controlled phase 3 trials
- Total 650 subjects aged 40 to 55 years
- Primary outcome: % gaining ≥3 lines in mesopic, high contrast, binocular DCNVA from baseline to day 30

CSF-1

- Phase 2b study, 166 subjects
- Primary endpoint met statistically significant improvement in DCNVA ≥3 lines
- Acceptable safety and tolerability

#### **Emerging Treatments—Miotics**

#### Pilocarpine Picodispenser (1 & 2 %)

- Uses MicroLine, a proprietary microdose formulation
- Improves near vision for 3 to 4 hours
  Plans to initiate two phase 3 trials (VISION-1 and VISION-2)
- PRX-100 (Acceclidine)
  - Acceclidine is a similar miotic to pilocarpine
  - Designed to induce strong miosis without associated accommodative distance blur
  - Phase 2b study of 58 patients aged 48 to 64 years

 Monocular distance-corrected near acuity increased ≥3 lines at 1 hour in 47% and by ≥2 lines in 92%

- ~50% maintained a 2-line or greater improvement in DCNVA for up to 7 hours
- Onset within 30 min, no significant loss in monocular BCDVA

#### **Emerging Treatments—Miotics**

#### Carbechol + Brimonidine

- Combination contributing effects
- Improves near vision for 7-8 hours
  In phase IIb
- In phase lib

#### Pilo (0.4%) + Nyxol

- Combination contributing effects
- Improves near vision for 8-10 hours
   Two drop formulation with Nyxol QHS
- Starting phase III

#### Using Pupillary Miotics to Improve DoF

- Pupillary miosis can improve near vision
   Distance vision can be lost if pupil becomes too small
- What is the optimal pupil size to increase DoF?

No specific number

- Optimal pupil size is a % of an individual's natural pupil size
- Lighting conditions and age influence the ability of pupil to increase DoF

# Effects of Light Conditions and Pupil Size on Near Vision (Xu et al. *IOVS*. 2016)

- Examined impact of small pupils and light levels on reading performance in distance-corrected presbyopes (n = 20; age 40-60 years)
- Low-light levels are detrimental to reading at near distances
- Near vision alleviated without loss of distance vision with:
  - Pupil sizes between 2.1 mm and 3.6 mm (not true for pupil size of 1 mm)
  - Multifocal treatments (contact lenses)
    Increasing light levels (140 and 1.4 cd/m<sup>2</sup>)
  - · Increasing light levels (140 and 1.4 cu/m-
- Poor light levels motivate emerging presbyopes to seek near reading aids











# What Do you Need to Succeed

- Significant number of patients may be new, who have only purchased reading glasses online or at big box retail stores
- Need to start educating patients now
- Must dilate and record findings on first exam before starting miotics
- Wide field imaging (confocal or ultra-wide field)
- Pupil testing for baseline (and follow-up in patients who don't respond)

# Confocal imaging















# What is it...

- EyeKinetix is an objective machine vision alternative to the SFM for assessing APDs
- Objectively assess pupils in less than 1 minute; an order of magnitude more detailed than the finest human observer
- It includes a scotopic / photopic pupil measurement + PD



# Test: Full Field Stimuli

Analog of Swinging Flashlight

Expanded Stimuli





## **Key Clinical Papers**

- There is evidence that very subtle APDs (above 0.3) are present in the vast majority of glaucoma subjects 1
- · Studies have shown that automated objective pupillography identified more than twice as many RAPDs than the SFM<sup>2</sup>
- Clinically detected asymmetry in disc damage was missed 49% of the time with the SFM compared to 21% with automated objective pupillography^2
- When using automated objective pupillography, the pupillary light reflex is strongly correlated with VF functional testing and measurements of RNFL thickness<sup>3</sup>

 Tatham, A.J., Meira-Freitas, D., Weinreb, R.N., Marvasti, A.H., Zangwill, L.M. and Medeiros, F.A., 2014. Estimation of retinal ganglion cell loss in glaucomatous eyes with a relative afferent pupillary defect. Investigative ophthalmology & visual ganglion cell loss in glascomatous spes with a relative afferent pupillary detect. Investigative opinitananousy in non-sience, 55(1), posi35-322.
2. Ali, M., Lu, Martinez, P., Farja, B., Gupta, L., Zhang, A., Hwang, E., Moster, M. and Spaeth, G. 2012. Pupil-based detection of symmetric glascomato dimage: comparison of the Kona RAPON pupillergible, winging flashight method, and magnifier-assisted swinging flashight method. Investigative Ophtholmology & Visual Science, 54(15), pp.4811-4811.

## **Potential Practice Concerns About Drops**

- Drop likely to be an adjunctive treatment— • Won't eliminate glasses
- Patients will likely want to use a drop periodically • Potential cons of drops: costs, cosmetic side effects (e.g. small pupil size in light-colored eyes), adherence
- Some will have adverse events like HA's, burning etc. • Helpful to start identifying ideal candidates and how drops
- could benefit practice over time

# **Opportunities for a Practice**

- Practice builder for any eye care provider
- · Access patients we don't normally see (reading glasses purchasers)
- Raise awareness to bring patients in for the treatment
  - · Retains patients
  - Raises patient interest in a presbyopia-correcting solutions
    - Spectacles
    - Contact lenses
    - Surgery
    - Therapeutics

# Thank you