FIRST-LINE THERAPY OPTIONS FOR PRIMARY OPEN-ANGLE GLAUCOMA
Definition of Glaucoma

• Family of ocular diseases characterized by progressive optic neuropathy and visual field loss
  – Gradual optic disk cupping
  – Associated visual field deficits
  – Progressive retinal ganglion cell loss
• No longer defined alone by elevated intraocular pressure (IOP)
Risk Factors

• Risk factors for the development and progression of glaucoma
  – Elevated IOP
  – Family history
  – Advanced age
  – Race
  – Genetic factors
Therapy for Glaucoma

• The primary strategy for treatment is reducing IOP
  – Data show importance of reducing IOP significantly
Treatment Significantly Delays Disease Progression

- The Early Manifest Glaucoma Trial (EMGT) outcomes showed that each 1 mm Hg reduction in intraocular pressure (IOP) reduces the risk of disease progression by 10%\textsuperscript{1}.

\textsuperscript{1} Heijl et al. Arch Ophthalmol. 2002
### Glaucoma Clinical Trials: IOP Lowering and Progression

<table>
<thead>
<tr>
<th>Study</th>
<th>IOP Reduction</th>
<th>% Progression Tx/no Tx</th>
</tr>
</thead>
<tbody>
<tr>
<td>OHTS(^1)</td>
<td>20% target</td>
<td>4.4%/9.5% (over 5 years)</td>
</tr>
<tr>
<td>EMGT(^2)*</td>
<td>25% (average)</td>
<td>45%/62% (over 6 years)</td>
</tr>
<tr>
<td>CNTGS(^3)</td>
<td>30% target</td>
<td>12%/35% (over 7 years)</td>
</tr>
<tr>
<td>CIGTS(^4) (med)</td>
<td>~35% (average)</td>
<td>Mean progression near 0</td>
</tr>
<tr>
<td>CIGTS(^4) (surg)</td>
<td>~48% (average)</td>
<td>Mean progression near 0</td>
</tr>
<tr>
<td>AGIS(^5)</td>
<td>&lt; 18 at all</td>
<td>Mean progression near 0</td>
</tr>
</tbody>
</table>

*10% reduction in risk with every 1 mm Hg of additional IOP lowering

Every Millimeter Matters

- **EMGT**: *Every mm Hg* of IOP reduction from baseline to month 3 decreased the risk of disease progression by 10%\(^1\)
- Every mm Hg counts, even in initial therapy of early glaucoma\(^1-3\)
- Similar reduction in risk in Ocular Hypertension Treatment Study (OHTS), The Advanced Glaucoma Intervention Study (AGIS), and Collaborative Normal-Tension Glaucoma Study (CNTGS)\(^3,4\)
  - Estimated 50% reduction in risk associated with a 3 mm Hg change in mean IOP (or *approximately 16% with each mm Hg*)\(^3\)

Consideration
When Selecting Therapy to Lower IOP

• Goals of primary therapy
  – The goal of primary therapy is to significantly lower IOP
  – Retain a high response rate—few to no non-responders
  – Maintain consistent diurnal pressure reduction
  – Encourage patient compliance and adherence by meeting patients’ goals and expectations

• Building-block approach to medical therapy
  – Establish the strongest foundation prior to resorting to adjunctive therapy
Potential Benefits of Monotherapy

- Encourages patient compliance\(^1,^2\)
- Decreased cost
- No added side effects
- It is worth taking the time to reach your target IOP with optimal monotherapy if at all possible
  - Need to explore all options
  - Few new options available in the future
  - Monotherapy unlikely to be retested

Option for Monotherapy

- Beta-blockers
- Alpha-agonists
- Carbonic anhydrase inhibitors
- Prostaglandin analogs
- Prostamide
- Miotic agents
Mechanism of Action

Increased Trabecular Outflow
- Miotics, Prostamides

Increased Uveoscleral Outflow
- Alphagan® P
- Prostaglandins
- Prostamides

Decreased Inflow
- Alphagan® P
- beta-blockers
- CAIs

Toris 1995, 1999
PGA Monotherapy as First-Line

- PGAs: an common choice for first-line therapy¹
  - IOP-lowering efficacy²-⁴
  - Sustained 24-hour control⁵
  - Once daily²-⁴
  - Few systemic side effects²-⁴

LUMIGAN®
(Bimatoprost Ophthalmic Solution)
as the First-Line Glaucoma Therapy
LUMIGAN®: Mechanism of Action

Increased Outflow

- Pressure-Insensitive
  (Presumed Uveoscleral)
- Pressure-Sensitive
  (Presumed Trabecular)

32% Reduction in IOP
(Lumigan 0.03% vs Timolol in Phase III FDA Trial)

Trabecular
35%

* 50%
Uveoscleral

*Brubaker et al AJO 2001;131
## LUMIGAN® 0.03% Studies Summary: Proven Superior Efficacy

<table>
<thead>
<tr>
<th>Author</th>
<th>Duration</th>
<th>Study</th>
<th>Mean Diurnal Baseline IOP (mm Hg)</th>
<th>P Value</th>
<th>Mean Diurnal IOP at Endpoint (mm Hg)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kammer et al(^1,2)</td>
<td>3 mos</td>
<td>Bimatoprost 0.03% (n = 131)</td>
<td>19.1 on latanoprost</td>
<td>.47</td>
<td>17.0</td>
<td>.02</td>
</tr>
<tr>
<td>Kammer et al(^1,2)</td>
<td>3 mos</td>
<td>Travoprost (n = 135)</td>
<td>18.9 on latanoprost</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cantor et al(^2,3)</td>
<td>6 mos</td>
<td>Bimatoprost 0.03% (n = 76)</td>
<td>23.1</td>
<td>.92</td>
<td>17.0</td>
<td>.03</td>
</tr>
<tr>
<td>Cantor et al(^2,3)</td>
<td>6 mos</td>
<td>Travoprost (n = 81)</td>
<td>23.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coleman et al(^2,4)</td>
<td>3 mos</td>
<td>Bimatoprost 0.03% (n = 90)</td>
<td>23.3</td>
<td>.54</td>
<td>17.4</td>
<td>.01</td>
</tr>
<tr>
<td>Coleman et al(^2,4)</td>
<td>3 mos</td>
<td>Cosopt(^6) (n = 87)</td>
<td>23.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higginbotham et al(^2,5)</td>
<td>12 mos</td>
<td>Bimatoprost 0.03% (n = 474)</td>
<td>24.7</td>
<td>.12</td>
<td>17.3</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Higginbotham et al(^2,5)</td>
<td>12 mos</td>
<td>Timolol (n = 241)</td>
<td>24.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manni et al(^6)</td>
<td>6 mos</td>
<td>Bimatoprost 0.03% (n = 28)</td>
<td>23.5 on timolol</td>
<td>NS</td>
<td>17.0</td>
<td>NS</td>
</tr>
<tr>
<td>Manni et al(^6)</td>
<td>6 mos</td>
<td>Latanoprost + Timoptic-XE(^6) (n = 28)</td>
<td>24.1 on timolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noecker et al(^2,7)</td>
<td>6 mos</td>
<td>Bimatoprost 0.03% (n = 133)</td>
<td>23.9</td>
<td>.19</td>
<td>16.9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Noecker et al(^2,7)</td>
<td>6 mos</td>
<td>Latanoprost (n = 136)</td>
<td>23.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katz et al(^8)</td>
<td>12 mos</td>
<td>Bimatoprost 0.01% (n = 186)</td>
<td>23.5</td>
<td>NS</td>
<td>17.3</td>
<td>NS</td>
</tr>
<tr>
<td>Katz et al(^8)</td>
<td>12 mos</td>
<td>Bimatoprost 0.0125% (n = 188)</td>
<td>23.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katz et al(^8)</td>
<td>12 mos</td>
<td>Bimatoprost 0.03% (n = 187)</td>
<td>23.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Length</th>
<th>Bimatoprost 0.03%</th>
<th>Bimatoprost 0.01%</th>
<th>Travoprost</th>
<th>Latanoprost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higginbotham et al¹</td>
<td>12 mos</td>
<td>44.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(bimatoprost 0.03% pivotal trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 483)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netland et al²</td>
<td>12 mos</td>
<td></td>
<td></td>
<td>49.5%</td>
<td>27.6%</td>
</tr>
<tr>
<td>(travoprost pivotal trial)</td>
<td></td>
<td></td>
<td></td>
<td>(n = 200)</td>
<td>(n = 196)</td>
</tr>
<tr>
<td>Noecker et al³</td>
<td>6 mos</td>
<td>44.4%</td>
<td></td>
<td></td>
<td>20.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 133)</td>
<td></td>
<td></td>
<td>(n = 136)</td>
</tr>
<tr>
<td>Parrish et al⁴</td>
<td>3 mos</td>
<td></td>
<td>68.6%</td>
<td>58.0%</td>
<td>47.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(n = 137)</td>
<td>(n = 138)</td>
<td>(n = 136)</td>
</tr>
<tr>
<td>Cantor et al⁵</td>
<td>6 mos</td>
<td>21.1%</td>
<td></td>
<td></td>
<td>14.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 76)</td>
<td></td>
<td></td>
<td>(n = 81)</td>
</tr>
<tr>
<td>Katz et al⁶</td>
<td>12 mos</td>
<td>37.4%</td>
<td></td>
<td>28.6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(n = 187)</td>
<td></td>
<td>(n = 185)</td>
<td></td>
</tr>
</tbody>
</table>

Introducing
the NEW PGA Monotherapy
LUMIGAN® 0.01%
(Bimatoprost Ophthalmic Solution)
for First-Line Glaucoma Therapy

Clinical Efficacy and Safety
Twelve-Month, Randomised, Controlled Trial of the Efficacy and Safety of Bimatoprost 0.01%, 0.0125%, and 0.03% in Patients With Glaucoma or Ocular Hypertension

• Clinical Efficacy and Safety vs Bimatoprost 0.03%
Introducing LUMIGAN® 0.01%

• **Bimatoprost 0.03%** is a well-established, safe, and effective medication used to **reduce intraocular pressure** (IOP) in glaucoma and ocular hypertension (OHT)

• A new formulation, **bimatoprost 0.01%**, was developed with the goal of creating a bimatoprost formulation that would **maintain the efficacy** of bimatoprost 0.03% and have **improved ocular surface tolerability**

• The formulation strategy was 2-fold:
  - **Reduce the concentration** of bimatoprost to 0.01% to decrease ocular surface drug exposure
  - **Increase transcorneal delivery** and **intraocular bioavailability** of bimatoprost
    
    Concentration of benzalkonium chloride increased to 200 ppm
    (the concentration used in latanoprost)
Phase 3 Study Methods

• Twelve-month study
  – Multicenter, double-masked, randomised, parallel, active-controlled trial
• Thirty-two US sites
  – LUMIGAN® 0.01% ophthalmic solution (n = 186);
  – LUMIGAN® 0.03%  (n = 187)
• Study population
  – Mean age: 63.5
  – 73% white, 14% black
  – ≈ 53% glaucoma diagnosis
  – 72% required washout
    • 36% prostaglandins
    • 15% bimatoprost

Phase 3 Study Endpoints

• **Primary endpoints**
  – Mean IOP assessed using equivalence analysis
    • Equivalence claimed if the 95% (or 97.5%) CIs of the between-group differences in mean IOP within ± 1 mm Hg at all timepoints and within ± 1 mm Hg at the majority of timepoints
    – Mean change from baseline IOP assessed using combined tests of noninferiority/superiority

• **Safety measures**
  – Adverse events
    • Macroscopic hyperaemia
    • Discontinuations due to adverse events

97.5% CI used as needed to correct for multiple comparisons (bimatoprost 0.01% and 0.0125% vs bimatoprost 0.03%).

Mean IOP at Month 12

Baseline mean IOP comparable between groups
LUMIGAN® 0.01%: 25.1, 23.0, 22.3 (8 AM, 12 PM, 4 PM; mm Hg)
LUMIGAN® 0.03%: 25.0, 23.2, 22.3 (8 AM, 12 PM, 4 PM; mm Hg)

Baseline mean diurnal IOP comparable between groups

Bimatoprost 0.01%: 23.5 mm Hg
Bimatoprost 0.03%: 23.5 mm Hg
Mean IOP Over 12 Months

LUMIGAN® 0.01% ophthalmic solution (n = 186)

LUMIGAN® 0.03% ophthalmic solution (n = 187)

Mean Change From Baseline IOP

- When adjusting for baseline, bimatoprost 0.01% was noninferior to bimatoprost 0.03% in IOP-lowering efficacy
  - Upper limit of the 95% CI of the between-group difference in mean change from baseline IOP $\leq 1.5$ mm Hg at all 17 timepoints

- The overall difference in mean change from baseline IOP across all 17 timepoints was 0.43 mm Hg with an upper confidence limit of 0.85 mm Hg (ANCOVA)
Overall Discontinuations

- LUMIGAN® 0.03% ophthalmic solution (n = 25/187): 13.4%
- LUMIGAN® 0.01% ophthalmic solution (n = 15/186): 8.1%

1. LUMIGAN® 0.01% and 0.03% [package insert]; 2. Katz et al. Am J Ophthalmol. 2010.
Similar Overall Safety Profile

Treatment-Related Ocular Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>LUMIGAN® 0.03% (n = 187)</th>
<th>LUMIGAN® 0.01% (n = 185)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>50.8%</td>
<td>38.4%</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>1.6%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Eye irritation</td>
<td>3.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Growth of eyelashes</td>
<td>3.8%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Erythema of eyelid</td>
<td>4.3%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Skin hyperpigmentation</td>
<td>5.3%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Eye pruritus</td>
<td>2.2%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Punctate keratitis</td>
<td>1.6%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Iris hyperpigmentation</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

*Statistically significant.

Incidence of Moderate to Severe Hyphaema

<table>
<thead>
<tr>
<th>Percentage of Patients Experiencing Hyphaema Between Visits</th>
<th>LUMIGAN® 0.03% ophthalmic solution (n = 17/187)</th>
<th>LUMIGAN® 0.01% ophthalmic solution (n = 6/185)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9.1%</td>
<td>3.2%</td>
</tr>
</tbody>
</table>

\(^aP = .019\)

Discontinuation Due to Ocular Adverse Events

Statistically significant.

LUMIGAN® 0.03% ophthalmic solution (n = 12/187)

LUMIGAN® 0.01% ophthalmic solution (n = 4/185)

6.4% 2.2%

*aP = .043

Conclusions

• **Efficacy**
  – LUMIGAN® 0.01% provides proven efficacy equivalent to bimatoprost 0.03%
    • Strict criteria for equivalent efficacy throughout the 12-month study
    • Up to a 30% IOP reduction from baseline over 12 months

• **Safety**
  – LUMIGAN® 0.01% ophthalmic solution is well tolerated attributable to the 67% reduction in drug concentration
    • Lower incidence of treatment-related adverse effects
    • Favorable hyperaemia profile
    • Low discontinuation rate due to ocular adverse events

First experiences with Lumigan 0.01% in Europe

- In real clinical practice
- Large population
Multicenter, prospective, open-label, observational study of bimatoprost 0.01% in patients with primary open-angle glaucoma or ocular hypertension

Methods: patients and study design

• Patients
  • n = 10,337
  • Primary open-angle glaucoma
  • Ocular hypertension

• Study
  • Multicentre
  • Open-label
  • Observational

10,337 patients with POAG or OH from 1334 centres in Germany
Patients naive to or on prior therapy

Treatment: Lumigan® 0.01%
(bimatoprost 0.1 mg/ml)
alone or in combination therapy as
determined by their physician

Baseline: Visit 1

10–14 weeks: Visit 2
Study assessments

• Change in IOP
• Target IOP
• Tolerability and continuation of bimatoprost 0.01% therapy
  – Physician and patients
• Additional IOP-lowering medication
• Early study discontinuation
• Adverse effects

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
Results: demographics

<table>
<thead>
<tr>
<th></th>
<th>Mean ±SD</th>
<th>n</th>
<th>% of received data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>67.3 ±12.3</td>
<td>10,195</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>4307</td>
<td>41.9</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>5978</td>
<td>58.1</td>
</tr>
<tr>
<td>Time since first diagnosis, years</td>
<td>4.0 ±4.9</td>
<td>9046</td>
<td></td>
</tr>
<tr>
<td>Diagnosis*: POAG</td>
<td></td>
<td>8645</td>
<td>83.8</td>
</tr>
<tr>
<td></td>
<td>OH</td>
<td>1666</td>
<td>16.2</td>
</tr>
<tr>
<td>Baseline IOP, mmHg: Right eye</td>
<td>20.1 ±4.5</td>
<td>10,275</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Left eye</td>
<td>20.1 ±4.5</td>
<td>10,287</td>
</tr>
</tbody>
</table>

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
Results: prior therapy I

<table>
<thead>
<tr>
<th>Medication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-blockers (monotherapy)</td>
<td>2730</td>
<td>32.3</td>
</tr>
<tr>
<td>Prostaglandin analogues</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumigan® 0.03% (monotherapy)</td>
<td>1008</td>
<td>11.9</td>
</tr>
<tr>
<td>Xalatan® (monotherapy)</td>
<td>1240</td>
<td>14.7</td>
</tr>
<tr>
<td>Travatan® (monotherapy)</td>
<td>690</td>
<td>8.2</td>
</tr>
<tr>
<td>Taflotan®</td>
<td>247</td>
<td>2.9</td>
</tr>
<tr>
<td>Carbonic anhydrase inhibitors</td>
<td>1679</td>
<td>19.9</td>
</tr>
<tr>
<td>α2 adrenergic agonists</td>
<td>596</td>
<td>7.1</td>
</tr>
</tbody>
</table>

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
Results: prior therapy II

- 1825 patients did not receive any prior therapy
- Of the 8441 patients receiving prior therapy, further analyses were performed in those receiving a β-blocker, bimatoprost 0.03%, latanoprost or travoprost as monotherapy

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
## Results: reasons for change

<table>
<thead>
<tr>
<th>Reason</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insufficient IOP control on prior therapy</td>
<td>52.6</td>
</tr>
<tr>
<td>Insufficient tolerability of prior therapy</td>
<td>28.7</td>
</tr>
<tr>
<td>Evidence of glaucomatous disease progression</td>
<td>12.7</td>
</tr>
<tr>
<td>Lack of compliance with prior therapy</td>
<td>7.9</td>
</tr>
<tr>
<td>Other reasons or missing data</td>
<td>21.4</td>
</tr>
</tbody>
</table>

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
Results: IOP according to previous monotherapy

![Bar chart showing IOP (mmHg) for various groups: All patients, Prior beta-blocker monotherapy, Prior Xalatan® monotherapy, Prior Travatan® monotherapy, Prior Lumigan® 0.03% monotherapy, No prior therapy.](image)

Adapted from Allergan data on file.
Results: IOP reduction from baseline according to prior therapy

According to the physician’s evaluation of efficacy, 70.3% of patients achieved an IOP that was at or below target IOP.

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
Results: adverse events, tolerability and compliance

- 93.9% of patients reported no adverse events
- Two severe adverse events were reported:
  - Acute exacerbation of chronic obstructive pulmonary disease
  - Asthma attack

---

Pfennigsdorf et al. Presented at COPHy 2011, Barcelona.
Conclusions-German study

- The greatest IOP reductions from baseline occurred in patients **without prior therapy**
- Significant IOP reductions were seen in patients previously treated with β-blocker, Xalatan® or Travatan® **monotherapy**
- Target pressure was reached in **70.3%** of patients
- Treatment was generally well tolerated (**no AEs reported in 94% of patients**)
- Bimatoprost 0.01% is a suitable **first-line** medication for the treatment of glaucoma
First experiences with Lumigan 0.01% in Mexico

-In real clinical practice
Efficacy and tolerability of bimatoprost 0.01% as monotherapy for patients with primary open-angle glaucoma or ocular hypertension: Lumigan RC Early Experience Design (LEED)

a multicentric study in Mexico

Curt Hartleben et al. Presented at 5th WGC 2013, Vancouver, Abstract 432, Poster P244
LEED in Mexico

• Topic:
  Efficacy and tolerability of bimatoprost 0.01% as monotherapy for patients with primary open-angle glaucoma or ocular hypertension: Lumigan RC Early Experience Design (LEED), a multicentric study in Mexico.

• Source:
  5th WGC 2013, Abs. 432; Poster P244

• Purpose:
  To evaluate efficacy and tolerability of bimatoprost 0.01% in Mexico.
  A multicenter study was designed where patients receiving first-line IOP-lowering drugs (prostaglandin analogs or beta-blockers) were switched to bimatoprost 0.01% without a washout period, as is usual in everyday clinical practice.
LEED in Mexico

• Method:
  – Open-label, multicenter, observational study
  – Patients with primary open-angle glaucoma (POAG) or ocular hypertension
  – Patients who previously had been using first-line medication (such as b-blocker, PGAs, or bimatoprost 0.03%) were switched to bimatoprost 0.01% for reduction of their IOP
  – Bimatoprost 0.01% was instilled nightly at 10 PM and IOP was measured at 10 AM ± 2 hours at 1 week and 1 and 3 months.
  – Patients and physicians assessed tolerability and satisfaction with both the old and the new regimen as well as ocular hyperemia measured against a photographic scale.
LEED in Mexico

• Results:
  – 896 eyes of 449 patients were recruited from 55 centers
  – Profile of patients: POAG: 83.7%, female: 64.2%

**Figure 1. IOP with bimatoprost 0.01% monotherapy in enrolled eyes**

4.1 mmHg
LEED in Mexico

- Results:

Figure 2. Percentage reduction from baseline in mean IOP at 3 months following initiation of bimatoprost 0.01% in all patients and in subgroups of patients based on previous monotherapy

- All patients
  - Bimatoprost 0.03%
  - Travoprost
  - Latanoprost
  - Timolol

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percentage of IOP Reduction from Baseline (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>-21.9</td>
</tr>
<tr>
<td>Bimatoprost</td>
<td>-14.7</td>
</tr>
<tr>
<td>Travoprost</td>
<td>-18.0</td>
</tr>
<tr>
<td>Latanoprost</td>
<td>-21.7</td>
</tr>
<tr>
<td>Timolol</td>
<td>-23.8</td>
</tr>
</tbody>
</table>

IOP, intraocular pressure.
LEED in Mexico

• Results:
  – Lower hyperemia overall after 3-month treatment
  – Moderate to severe hyperemia was reduced from 24% of patients to **8.1%**
  – At month 3,
    • **2.4 times less** moderate hyperemia
    • **4.5 times less severe hyperemia**
LEED in Mexico

• Results:
  – Satisfaction at month 3
    • 84.7% of patients rated more comfortable than previous treatment
    • 88.9% of physicians described as very convenient

Table 2. Patient and physician satisfaction

<table>
<thead>
<tr>
<th>Patient satisfaction with treatment</th>
<th>Initiation, %</th>
<th>Week 1, %</th>
<th>Month 1, %</th>
<th>Month 3, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=357)</td>
<td>(N=382)</td>
<td>(N=326)</td>
<td>(N=215)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>5.3</td>
<td>1.6</td>
<td>0.6</td>
<td>0.0</td>
</tr>
<tr>
<td>5–6</td>
<td>30.5</td>
<td>10.2</td>
<td>5.3</td>
<td>2.3</td>
</tr>
<tr>
<td>7–8</td>
<td>30.8</td>
<td>23.8</td>
<td>20.2</td>
<td>13.0</td>
</tr>
<tr>
<td>9–10</td>
<td>33.3</td>
<td>70.4</td>
<td>73.9</td>
<td>84.7</td>
</tr>
</tbody>
</table>

Physician satisfaction with treatment

<table>
<thead>
<tr>
<th>Physician satisfaction with treatment</th>
<th>Initiation, %</th>
<th>Week 1, %</th>
<th>Month 1, %</th>
<th>Month 3, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=351)</td>
<td>(N=378)</td>
<td>(N=316)</td>
<td>(N=216)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>6.8</td>
<td>0.3</td>
<td>0.3</td>
<td>0.9</td>
</tr>
<tr>
<td>5–6</td>
<td>25.4</td>
<td>6.3</td>
<td>3.5</td>
<td>1.9</td>
</tr>
<tr>
<td>7–8</td>
<td>31.1</td>
<td>19.0</td>
<td>9.2</td>
<td>8.3</td>
</tr>
<tr>
<td>9–10</td>
<td>36.8</td>
<td>74.3</td>
<td>87.0</td>
<td>88.9</td>
</tr>
</tbody>
</table>
• Conclusion:
  – Bimatoprost 0.01% is an effective IOP-lowering agent in patients receiving previous monotherapy including prostaglandin analogs and timolol.
  – After 1 and 3 months of use, it lowered IOP significantly from baseline levels.
  – Bimatoprost 0.01% was associated with a 3-fold reduction in hyperemia.
  – Patient and physician satisfaction was excellent.
LUMIGAN® 0.03%:  
The Heritage of  
LUMIGAN® 0.01%  

Clinical Summary
LUMIGAN® 0.03%
(Bimatoprost Ophthalmic Solution)

Summary of Efficacy and Safety Studies
# LUMIGAN® 0.03% Studies Summary: Proven Superior Efficacy

<table>
<thead>
<tr>
<th>Author</th>
<th>Duration</th>
<th>Study</th>
<th>Mean Diurnal Baseline IOP (mm Hg)</th>
<th>P Value</th>
<th>Mean Diurnal IOP at Endpoint (mm Hg)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kammer et al&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>3 mos</td>
<td>Bimatoprost 0.03% (n = 131)</td>
<td>19.1 on latanoprost</td>
<td>.47</td>
<td>17.0</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Travoprost (n = 135)</td>
<td>18.9 on latanoprost</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cantor et al&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td>6 mos</td>
<td>Bimatoprost 0.03% (n = 76)</td>
<td>23.1</td>
<td>.92</td>
<td>17.0</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Travoprost (n = 81)</td>
<td>23.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coleman et al&lt;sup&gt;2,4&lt;/sup&gt;</td>
<td>3 mos</td>
<td>Bimatoprost 0.03% (n = 90)</td>
<td>23.3</td>
<td>.54</td>
<td>17.4</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cosopt&lt;sup&gt;®&lt;/sup&gt; (n = 87)</td>
<td>23.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higginbotham et al&lt;sup&gt;2,5&lt;/sup&gt;</td>
<td>12 mos</td>
<td>Bimatoprost 0.03% (n = 474)</td>
<td>24.7</td>
<td>.12</td>
<td>17.3</td>
<td>&lt; .001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Timolol (n = 241)</td>
<td>24.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manni et al&lt;sup&gt;6&lt;/sup&gt;</td>
<td>6 mos</td>
<td>Bimatoprost 0.03% (n = 28)</td>
<td>23.5 on timolol</td>
<td>NS</td>
<td>17.0</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Latanoprost + Timoptic-XE&lt;sup&gt;®&lt;/sup&gt; (n = 28)</td>
<td>24.1 on timolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noecker et al&lt;sup&gt;2,7&lt;/sup&gt;</td>
<td>6 mos</td>
<td>Bimatoprost 0.03% (n = 133)</td>
<td>23.9</td>
<td>.19</td>
<td>16.9</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Latanoprost (n = 136)</td>
<td>23.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katz et al&lt;sup&gt;8&lt;/sup&gt;</td>
<td>12 mos</td>
<td>Bimatoprost 0.01% (n = 186)</td>
<td>23.5</td>
<td>NS</td>
<td>17.3</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bimatoprost 0.0125% (n = 188)</td>
<td>23.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bimatoprost 0.03% (n = 187)</td>
<td>23.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Length</th>
<th>Bimatoprost 0.03%</th>
<th>Bimatoprost 0.01%</th>
<th>Travoprost</th>
<th>Latanoprost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higginbotham et al¹</td>
<td>12 mos</td>
<td>44.7% (n = 483)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(bimatoprost 0.03% pivotal trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netland et al²</td>
<td>12 mos</td>
<td></td>
<td>49.5% (n = 200)</td>
<td>27.6% (n = 196)</td>
<td></td>
</tr>
<tr>
<td>(travoprost pivotal trial)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noecker et al³</td>
<td>6 mos</td>
<td>44.4% (n = 133)</td>
<td></td>
<td>20.6% (n = 136)</td>
<td></td>
</tr>
<tr>
<td>Parrish et al⁴</td>
<td>3 mos</td>
<td>68.6% (n = 137)</td>
<td>58.0% (n = 138)</td>
<td>47.1% (n = 136)</td>
<td></td>
</tr>
<tr>
<td>Cantor et al⁵</td>
<td>6 mos</td>
<td>21.1% (n = 76)</td>
<td></td>
<td>14.8% (n = 81)</td>
<td></td>
</tr>
<tr>
<td>Katz et al⁶</td>
<td>12 mos</td>
<td>37.4% (n = 187)</td>
<td>28.6% (n = 185)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Summary

• Building-block approach to medical therapy
  – Establish the strongest foundation prior to resorting to adjunctive therapy
  – Maximize monotherapy
    • Target IOP should be reached with the minimal number of medications as possible
• LUMIGAN® 0.03% (bimatoprost ophthalmic solution) has a proven record of efficacy in lowering IOP over the long term more than any other single medication available for glaucoma management1-11
• LUMIGAN® 0.01% (bimatoprost ophthalmic solution) is a new therapeutic option
  – As effective as LUMIGAN® 0.03% in lowering IOP with improved tolerability and safety profile
  – First choice option for patients beginning PGA therapy

Indication

LUMIGAN® 0.01% (bimatoprost ophthalmic solution) is a prostaglandin analog indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

Please refer to accompanying full prescribing information.
Important Safety Information

Warnings and Precautions:
Bimatoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as bimatoprost is administered.

Important Safety Information continued on next slide.
Important Safety Information (Continued)

Warnings and Precautions (continued): After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

Important Safety Information continued on next slide.
Important Safety Information (Continued)

**Adverse Reactions:** In clinical studies with bimatoprost ophthalmic solutions (0.01% or 0.03%), the most common adverse event was **conjunctival hyperemia** (range 25%-45%). Other common events (> 10%) included **growth of eyelashes** and **ocular pruritus**.

Please refer to full prescribing information.
Summary

Indication:
LUMIGAN® 0.01% (bimatoprost ophthalmic solution) is a prostaglandin analog indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

Administration:
one drop in the affected eye(s), once daily in the evening

Please refer to full prescribing information.
FIRST-LINE THERAPY OPTIONS FOR PRIMARY OPEN-ANGLE GLAUCOMA
Thank You