**Treatment of Eyebrow Hypotrichosis Using Bimatoprost: A Randomized, Double-Blind, Vehicle-Controlled Pilot Study**

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**BACKGROUND** The Food and Drug Administration has approved bimatoprost ophthalmic solution (0.03%) for the treatment of eyelash hypotrichosis. Previous reports of its efficacy in eyebrow hypotrichosis are anecdotal.

**OBJECTIVE** To assess the efficacy and safety of bimatoprost 0.03% ophthalmic solution applied to the eyebrows in a randomized, double-blind, vehicle-controlled study.

**METHODS** Subjects (n = 20) with mild to moderate eyebrow hypotrichosis enrolled in the study. One group (Bim) applied bimatoprost to each eyebrow daily for 9 months, and another applied vehicle nightly to each eyebrow for 5 months. Subjects in the latter group were re-randomized to apply bimatoprost (Veh-Bim Group) or vehicle (Veh Group) daily to each eyebrow for 4 months. The primary end point was investigator-assessed eyebrow appearance; secondary end points were subject-reported outcomes.

**RESULTS** Investigator assessments showed significant improvements from baseline to 6 (p = .002) and 7 (p = .005) months for the eyebrows treated with bimatoprost. p-Values for the Veh-Bim and Veh groups were not significant at any time point. End-of-study subject satisfaction with eyebrow fullness or thickness and darkness or color was greater in the Bim group than in the Veh group. Adverse effects were not observed.

**CONCLUSION** Bimatoprost 0.03% ophthalmic solution applied daily for 9 months improves the appearance of eyebrows noticeably more than vehicle, without side effects.

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The use of bimatoprost ophthalmic solution to treat ocular hypertension and to control the progress of glaucoma has been evaluated in numerous clinical trials.1,2 Investigators3,4 also noted that bimatoprost stimulated the growth of eyelashes, which led to Food and Drug Administration approval of the ophthalmic solution for the treatment of eyelash hypotrichosis.5 Research has since shown that, in patients with hypotrichosis, bimatoprost 0.03% ophthalmic solution increases eyelash length, thickness, and darkness.5,6 Animal studies show that bimatoprost, a structural prostaglandin analog, increases the fraction of hair follicles in the anagen phase and prolongs the duration of the anagen phase. These changes result in an altered eyelash hair cycle. Bimatoprost appears to increase the size of the dermal papilla and hair bulb. These may explain its effect on eyelash thickness and fullness.7 Most patients reported longer eyelashes and darker color after using bimatoprost daily for 12 weeks.5

Full eyebrows and eyelashes make the face look more cosmically attractive.5 Although making seemingly minor contributions to the overall facial appearance, eyebrows and eyelashes help to frame the face. Elias and colleagues8 reported two cases of successful stimulation of eyebrow growth using...
bimatoprost. One patient with thinning eyebrow hair applied bimatoprost to both eyebrows each night for 16 weeks. At the end of the treatment period, the patient reported improvement in the appearance of both eyebrows and was very satisfied with the result. Side effects were not observed. In the second case, a patient with an 8-year history of thinning eyebrow hair applied bimatoprost nightly for 12 weeks, with noticeable improvement and no side effects. The authors speculated that these encouraging results may be attributed to similarities in the hair cycles of eyebrows and eyelashes, both having anagen phases lasting only 1 to 2 months.

One year later, Schweiger and colleagues described a patient with sparse hair on the left lateral eyebrow. The patient applied bimatoprost to the left eyebrow once daily for 4 months. At 4 months, physical examination showed that the left eyebrow hair was denser, longer, and darker. The skin was slightly pigmented, and the eyelash had been treated as well. That same year, Suwanchatchai and colleagues showed that bimatoprost enhances eyebrows as effectively as minoxidil. These encouraging results suggest that bimatoprost ophthalmic solution enhances the appearance of eyebrows.

The purpose of the present study was to assess the efficacy and safety of bimatoprost 0.03% ophthalmic solution (Latisse; Allergan, Inc., Irvine, CA) applied to the lateral and medial eyebrows during and after 9 months of application in a randomized, double-blind, vehicle-controlled study.

**Methods**

**Subjects**

Subjects (*n* = 20 females) with a mean age ± standard deviation of 57.6 ± 9.5 with mild to moderate hypotrichosis (score 3 or 4 on the 4-point Beer Global Eyebrow Assessment (GEyA) scale) of both eyebrows enrolled in the eyebrow study. Patient histories indicated the absence of conditions (e.g., hypo- or hyperthyroidism) that would interfere with the efficacy of the treatment product. The GEyA score (described below) enables investigators to objectively compare the eyebrow appearance of a given subject with known standards. The scale was developed by examining numerous subjects with mild to severe hypotrichosis. The GEyA tool considers darkness, thickness, and length of eyebrow hair, providing a global assessment of eyebrow appearance.

Subjects were not permitted to treat eyebrows using alternative methods during the study. Those of childbearing potential had a negative pregnancy test result at baseline and were required to practice an acceptable method of birth control throughout the study. Exclusion criteria were pregnancy, breast feeding, plans to become pregnant, uncontrolled systemic disease, eyebrow disorder, trichotillomania disorder, glaucoma or high ocular pressure, use of ocular pressure-lowering prostaglandin analogs, hypersensitivity to treatment products, previous cosmetic surgery of the upper face, permanent eye or eyebrow makeup, application of eyebrow tint or dye within 2 months before the start of the study, planned facial cosmetic procedure that would affect study results, or participation in an investigational drug or device study within the previous 30 days. The study was approved by an institutional review board (Clinical trials no. NCT01387906), and all subjects provided signed informed consent to treatment and photography.

**Procedure**

At the first visit, subjects were randomized to receive a 1-month supply of bimatoprost 0.03% ophthalmic solution or vehicle (lubricant eye drops, Refresh Tears; Allergan, Inc.). Treatment products (bimatoprost or vehicle) were identically packaged and dispensed monthly for 9 months total. Subjects of one treatment group (Bim) applied 1 drop of bimatoprost to each eyebrow daily for 9 months, and subjects of a second treatment group applied vehicle nightly to each eyebrow for 5 months. Subjects in the second group were then re-randomized to apply bimatoprost...
(Veh-Bim group) or vehicle (Veh group) daily to each eyebrow for the remaining 4 months. During that period, there were three treatment groups: Bim group, Veh-Bim group, and Veh group. Subjects were not allowed to groom but were permitted to apply makeup after the treatment product (Bim or Veh) had been applied and allowed to dry. Subjects failing to apply treatment product more than four times were removed from the study. Photographs (Visia; Canfield Scientific, Fairfield, NJ) were taken under standardized conditions of position and lighting at each visit. The study began in March 2011 and was completed in March 2012.

**Efficacy and Safety**

The investigator used the GEyA to evaluate eyebrow growth at each visit according to a 4-point scale (1 = maximal growth, eyebrows very thick and very dark in color; 2 = marked growth, eyebrows thick and medium to dark in color; 3 = moderate growth, eyebrows moderately thick and light to medium in color; and 4 = minimal to no growth, eyebrows thin and light in color). Subjects rated satisfaction with hair density, darkness, and thickness by completing a patient-reported outcomes questionnaire (Tables 1 and 2) similar to that of Yoelin and colleagues at each visit. GeyA scores, patient-reported outcomes, and adverse events were evaluated at each visit.

**Data Analysis**

Data were tabulated, graphed, and tested for significant differences using the Pearson chi-square test. Data were analyzed on an intention-to-treat basis. Because multiple comparisons were made with baseline, Bonferroni correction was applied to the cut-off level. Nine comparisons were made with baseline so the corrected cut-off level for significance was .05/9 = .0055.

Efficacy in eyebrow fullness was evaluated using two methods: change in GEyA score from baseline and responder analysis. A responder was a subject with an at least 1-grade improvement (increase) from baseline.

**Results**

**Global Eyebrow Assessment**

At each time point, the investigator assessed the appearance of the right and left eyebrows using the

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>How satisfied are you with the Fullness or thickness of your eyebrows</td>
<td>Very satisfied, satisfied, neutral, unsatisfied, very unsatisfied</td>
</tr>
<tr>
<td>Darkness of your eyebrows</td>
<td>Very satisfied, satisfied, neutral, unsatisfied, very unsatisfied</td>
</tr>
<tr>
<td>Eyebrows overall</td>
<td>Very satisfied, satisfied, neutral, unsatisfied, very unsatisfied</td>
</tr>
<tr>
<td>Rate your eyebrow Fullness or thickness</td>
<td>Very full or thick, full or thick, medium, thin, very thin</td>
</tr>
<tr>
<td>Overall color</td>
<td>Very dark, dark, medium, light, very light</td>
</tr>
<tr>
<td>I am concerned about The amount of time I spend filling in my eyebrows</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
<tr>
<td>The amount of time to make my eyebrows presentable daily</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
<tr>
<td>How tired my eyes look without makeup</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
<tr>
<td>My eyebrows without makeup applied Make my eyes look tired</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
<tr>
<td>Make me feel confident in my looks</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
<tr>
<td>Make me feel attractive</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
</tbody>
</table>
GEyA scale. The scores of the right and left eyebrows did not differ significantly at each time point (Wilcoxon signed rank test), so the average of the right and left eyebrow scores was used in the analyses. Differences from baseline were significant at 6 (p = 0.002) and 7 (p = 0.005) months for the Bim group. These are the same months that peak percentages of subjects were observed for the Bim group (Figure 1). p-Values for all other time points were not significant for the Bim group, and p-values for the Veh-Bim and Veh groups were not significant at any time point.

Figure 1 shows the mean change in GEyA score from baseline according to visit and treatment group. The Bim group shows increasing improvement across visits, with peaks at 4, 7, and 9 months. Veh subjects who crossed over to bimatoprost at month 5 showed a change in scores at months 6, 7, 8, and 9. Veh-Bim group scores were higher than those of the Veh group at months 6, 8, and 9.

In the responder analysis (Figure 2), the Bim responder rate ranged from 77.8% to 100% from months 6 through 9, compared with 50% to 75% for the Veh-Bim group and 25% to 75% for the Veh group during the same period.

Subject satisfaction with fullness and thickness, eyebrow darkness and color, and specific issues of convenience in use and attractiveness is presented in Figure 3 through 12. Clinical examples are presented in Figure 4, a Bim subject, and Figure 5, a Veh subject.

**Table 2. Additional Questions at End of Study**

<table>
<thead>
<tr>
<th>Question</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>After using the study drug I have noticed significant improvement in</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
<tr>
<td>The fullness of my eyebrows</td>
<td></td>
</tr>
<tr>
<td>The darkness of my eyebrows</td>
<td>Very much agree, agree, neutral, disagree, very much disagree</td>
</tr>
</tbody>
</table>

**End-of-Study Comments**

**Improvement in Eyebrow Fullness**

In the Bim group, 50% of subjects reported significant improvement in the fullness of their eyebrows at 9 months (Table 3). In the Veh-Bim group and Veh group, 25% of subjects reported significant
improvement. Correspondingly, the percentage of subjects reporting little or no significant improvement was lowest (12%) in the Bim group and highest (75%) in the Veh group.

**Improvement in Eyebrow Darkness**
As shown in Table 4, 50% of subjects in the Bim group, 60% in the Veh-Bim group, and 0% in the Veh group reported significant improvement in eyebrow darkness at 9 months. The higher percentage of subjects in the Veh-Bim group (60%) than in the Bim group (50%) may be an early effect of the bimatoprost at 6 months (Figure 1). None of the subjects in the Veh group reported significant improvement in eyebrow darkness.

**Adverse Effects**
Adverse effects were not observed in this study. Those reported with the use of bimatoprost 0.03% ophthalmic solution used to enhance eyelash growth include eye redness, itchiness, dryness, tightness, and burning; periorbital redness and pigmentation changes; and eyelid redness. Others were eye pruritus, conjunctival hyperemia, eye irritation, dry eye symptoms, erythema, and hyperpigmentation of the eyelids. In a large clinical trial, conjunctival hyperemia was the only adverse effect whose incident rate was significantly higher with bimatoprost than with vehicle. These were not observed in any subject in the present study.

<table>
<thead>
<tr>
<th>Category</th>
<th>Bim</th>
<th>Veh-Bim</th>
<th>Veh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agree or very much agree</td>
<td>4 (50)</td>
<td>1 (25)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Neutral</td>
<td>3 (38)</td>
<td>2 (50)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Disagree or very much disagree</td>
<td>1 (12)</td>
<td>1 (25)</td>
<td>3 (75)</td>
</tr>
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Bim, bimatoprost; Veh, vehicle.
Discussion

To the authors’ knowledge, this is the first randomized, double-blind, vehicle-controlled study of the efficacy and safety of bimatoprost 0.03% ophthalmic solution to enhance eyebrow appearance. The results discussed below are consistent with those of earlier studies\textsuperscript{5,8,9} in which bimatoprost was applied for only 3 or 4 months, as opposed to 9 months in the present study.

As shown in Figure 1, the increase in GEyA score of the Veh group occurred early, during the first several months, and changed little until 6 months, when it began to rise higher. The authors attribute this increase to a change in eyebrow thickness due to the requirement that subjects not groom eyebrows (see Methods) during the study. Without grooming, eyebrow thickness would be expected to increase without treatment. This effect will hereafter be referred to as the “nongrooming effect.” In the Bim group, the increase in GEyA score began to rise at 2 to 3 months, much earlier than the vehicle score, which began to rise at 6 months. When bimatoprost was added to the Veh-Bim subjects’ regimen (after 5 months), the change in GEyA score in the Veh-Bim group began to increase within 2 months and continued to rise, similar to that observed in the Bim group during the first several months. This confirms the presence of a Bim treatment effect.

The GEyA and responder analysis data indicate that maximum eyebrow improvement occurred at 6 to 7 months when bimatoprost was applied daily for 9 months, although Figures 1 and 2 show clearly that the bimatoprost effect on the eyebrows is greater than the nongrooming effect throughout the study. The significant differences at 6 and 7 months from baseline for the Bim group support this; a significant difference from baseline was not observed at any time for the Veh group.

Overall subject satisfaction with eyebrows was consistently higher in the Bim group than in the Veh or Veh-Bim group (Figure 6). The borderline significant difference ($p = .0054$) from baseline at 9 months for only the Bim group supports this.

In the Bim group, subject satisfaction with fullness and thickness (Figure 7) was greater for bimatoprost than for vehicle throughout the study period (Figure 3). Similar trends were observed in satisfaction with eyebrow darkness (Figure 8). For

### Table 4. Subject Responses to Whether Darkness of Eyebrows Had Improved Significantly at 9 Months

<table>
<thead>
<tr>
<th>Category</th>
<th>Bim (%)</th>
<th>Veh-Bim (%)</th>
<th>Veh (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agree-very much</td>
<td>4 (50)</td>
<td>3 (60)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Neutral</td>
<td>4 (50)</td>
<td>2 (40)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Disagree-very much</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Bim, bimatoprost; Veh, vehicle.
eyebrow color, subject color ratings with bimatoprost in the Bim group were greater than vehicle in the Veh group for 9 months (Figure 9), although the addition of bimatoprost to the Veh-Bim group at 6 months failed to increase the percentage of subjects rating their eyebrow color as dark.

For eyebrow darkness, the percentage of subjects satisfied to very satisfied was consistently higher in the Bim group than in the Veh-Bim or Veh groups (Figure 6). The bimatoprost appeared to be more effective in the Bim group than vehicle in the Veh group during the entire treatment period. The addition of bimatoprost to Veh-Bim group at 6 months was associated with the consistently higher percentage of subjects rating their eyebrow color as dark.

Regarding overall satisfaction with eyebrows, the percentage of subjects who were satisfied to very satisfied was consistently higher in the Bim group than in either of the other two treatment groups (Figure 6). The difference from baseline was borderline significant ($p = .0054$) at 9 months for the Bim group and nonsignificant at all time points for the other two groups. The addition of bimatoprost to the Veh-Bim group at 6 months was associated with an immediate increase only in the subjects in the Veh-Bim group. This increase persisted throughout the remainder of the study period but did not appear in the Veh group.

In the Bim group, subject concern about the time required to fill in eyebrows decreased as the study period progressed (Figure 10). As for stress to make eyebrows presentable each day (Figure 11), the Bim and Veh groups trended lower as the study period progressed. Subject concern about the eyes appearing tired without makeup (Figure 12) was consistently higher for the Veh group than for the Bim or Veh-Bim group.
Subject confidence in looks with no eyebrow makeup (Figure 13) was generally higher in the Bim group than in the Veh group. The Veh-Bim data suggest an initial nongrooming effect that disappeared at 7 months. Confidence in attractiveness with no eyebrow makeup (Figure 14) was initially erratic for the Bim group until 6 months, when it increased.

As shown in Table 3, 50% of subjects in the Bim group reported significant improvement in the fullness of their eyebrows at 9 months. In the Veh-Bim and Veh groups, 25% of subjects reported significant improvement. Correspondingly, the percentage of subjects reporting little or no significant improvement was lowest (12%) in the Bim group and highest (75%) in the Veh group.

Regarding eyebrow darkness (Table 4), 50% of subjects of the Bim group, 60% in the Veh-Bim group, and 0% in the Veh group reported significant improvement in the darkness of their eyebrows at 9 months. The higher percentage of subjects in the Veh-Bim group (60%) than in the Bim group (50%) may be an early effect of the bimatoprost at 6 months (Figure 2). None of the subjects in the Veh group reported a significant improvement in eyebrow darkness.

Skin hyperpigmentation associated with bimatoprost treatment of eyelashes, eyebrows, or ophthalmic conditions has been reported. In their study of eyelash growth, Smith and colleagues observed skin hyperpigmentation in more than 2% of subjects, but the percentage did not differ significantly from that of vehicle. Also studying...
eyelashes, Yoelin and coworkers\textsuperscript{2} noted periorbital pigmentation in five of 28 subjects (18%); in two of the five subjects, the darkening was described as possible, slight, or little. Schweiger and colleagues\textsuperscript{5} reported “slight skin pigmentation” in a single patient after 4 months of self-treating eyebrows with bimatoprost solution every other day. Law\textsuperscript{6} cited two references describing increases in periocular pigmentation after ophthalmic use of bimatoprost. Cohen\textsuperscript{7} cited several references (two in ophthalmology publications) in which eyelid pigmentation occurred after administration of bimatoprost as an eye drop for the treatment of ophthalmic conditions. Elias and coworkers\textsuperscript{8} described two cases of eyebrow growth after treatment with bimatoprost. Skin pigmentation was not observed in either patient. Suwanchatchai and colleagues\textsuperscript{9} compared eyebrow enhancement of bimatoprost with that of minoxidil and did not report skin pigmentation in any of the 27 patients who completed the study. Of the seven named references, three\textsuperscript{5,8,9} described the use of bimatoprost for eyebrow enhancement, and two of those\textsuperscript{8,9} did not report skin pigmentation. In contrast, the remaining references reported skin pigmentation when bimatoprost was used for ophthalmic purposes\textsuperscript{6,7} or to enhance eyelashes\textsuperscript{1,2}. One would expect a greater likelihood of adverse events with eyelash treatment than with eyebrow treatment because of the closer proximity of eyelashes to the eyelid skin. Skin pigmentation appears to occur more frequently when bimatoprost is used to treat ophthalmic conditions or to enhance eyelashes than when it is used to treat eyebrows. For these reasons, it is not surprising that subjects in the present study did not experience skin hyperpigmentation after treatment of their eyebrows with bimatoprost.

Limitations of the present study include the small number of subjects, the absence of data on inter- or intraobserver consistency in using the GEyA scale, and the assumptions that subjects adhered to the treatment schedule and to the directive that they not groom their eyebrows during the study period. The encouraging results justify additional studies with more patients to explore the most responsive patient population.

**Conclusion**

Bimatoprost 0.03% ophthalmic solution applied daily for 9 months improves the appearance of eyebrows noticeably more than vehicle, without side effects.

**References**


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