Supplementary material

Bacharach J, Tatham A, Ferguson G, Belalcázar S, Thieme H, Goodkin ML, Chen MY, Guo Q, Liu J, Robinson MR, Bejanian M, Wirta DL; on behalf of the ARTEMIS 2 Study Group. Phase 3, randomized, 20-month study of the efficacy and safety of bimatoprost implant in patients with open-angle glaucoma and ocular hypertension (ARTEMIS 2). *Drugs*.

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Online Resource 1

Patient Eligibility Criteria

Inclusion criteria

- Male or female, 18 years of age or older
- Signed documents related to data protection and privacy in accordance with relevant country and local requirements
- Provided written informed consent, is able to understand and follow study instructions, and is likely to complete all required visits and procedures
- Is willing to have IOP-lowering treatments withheld as required during washout period, and in the opinion of the investigator, could undergo washout without significant risk
- For women of childbearing potential, pregnancy test administered at baseline must be negative
- Diagnosis of OAG or OHT in each eye, with both eyes requiring IOP-lowering treatment (diagnosis did not have to be the same in both eyes)
- In the investigator's opinion, both eyes could be treated adequately with topical ophthalmic beta-blocker (eg, timolol) eye drops as the sole therapy
- In the investigator's opinion, both eyes could be treated adequately with topical PGA (eg, bimatoprost, latanoprost, travoprost) eye drops as the sole therapy
- Iridocorneal angle in the study eye confirmed to have Shaffer grade of ≥3 on clinical gonioscopy of the inferior angle and peripheral anterior chamber depth by Van Herick examination confirmed to be ≥1/2 corneal thickness by agreement of 2 independent ophthalmologists*
- Patient was washed out of all IOP-lowering medications at the baseline visit
- At the baseline visit, IOP in the study eye of ≥22 and ≤32 mmHg at hour 0, and ≥19 and ≤32 mmHg at hour 2
- At the baseline visit, IOP in the fellow eye of ≤32 mmHg at hour 0 and hour 2
- Central CECD by specular microscopy was ≥1800 cells/mm^2 in at least 1 eye by automated analysis at screening, and by baseline, central CECD in both eyes was confirmed as being qualified by the CRC, with at least 1 eye qualified for inclusion as the study eye
- Baseline BCVA (Snellen equivalent, by manifest refraction) of 20/50 or better in the study eye and 20/100 or better in the fellow eye

Exclusion criteria

Nonocular criteria

- Uncontrolled systemic disease
- Female patients who are pregnant, nursing, planning a pregnancy during the study, or of childbearing potential and not using a reliable method of contraception
- Known allergy or sensitivity to any study medication or component, any component of the delivery vehicle, procedure-related materials, or diagnostic agents used during the study (eg, topical anesthetic, dilating drops, fluorescein)
- Any contraindication to beta-blocker therapy (eg, reactive airway disease, sinus bradycardia, etc)
- Any condition that could preclude the patient's ability to comply with study requirements, including completion of the study
- Patient has a condition or is in a situation which, in the investigator's opinion, could put the patient at significant risk, confound the study results, or interfere significantly with the patient's participation in the study
- Anticipated use of oral, intramuscular, or intravenous corticosteroids from 2 months prior to baseline through week 52
- Concurrent or anticipated enrollment in an investigational drug or device study or participation in such a study within 2 months prior to the baseline visit through the final study visit
- Previous enrollment in another Allergan bimatoprost implant study

- Known history of a bleeding disorder or prolonged bleeding after surgery (in the opinion of the investigator); patients receiving pharmacologic blood thinners (eg, aspirin or Coumadin) could be enrolled at the investigator's discretion

Ocular criteria

- In the investigator's opinion, the patient was nonresponsive to topical ophthalmic beta-blockers and/or topical PGAs
- History or evidence of clinically relevant, substantial ocular trauma (eg, a traumatic cataract, traumatic angle recession, etc) in the study eye
- History or evidence of complicated cataract surgery in the study eye (eg, surgery resulting in complicated lens placement such as anterior chamber intraocular lens, sulcus intraocular lens, aphakia, etc) or intraoperative complications (such as a posterior capsular tear, substantial iris trauma, etc)
- History of phakic intraocular lens insertion for refractive error correction in the study eye
- Intraocular surgery (including cataract surgery) or ocular laser surgery within the 6 months prior to treatment (day 1) in the study eye
- History of corneal graft, including partial grafts (eg, Descemet membrane endothelial keratoplasty, Descemet stripping endothelial keratoplasty) in the study eye
- Incisional refractive surgery (eg, radial keratotomy) other than astigmatic keratotomy or limbal relaxing incisions in the study eye
- Corneal or other ocular abnormalities in either eye that could preclude accurate readings with an applanation tonometer, AS-OCT, specular microscope, and/or a contact pachymeter or that could confound study results (eg, moderate to severe corneal dystrophy including anterior basement membrane dystrophy [ie, map-dot-fingerprint] and guttata; mild anterior basement membrane dystrophy or mild guttata by clinical examination were not exclusionary if, in the opinion of the investigator, the condition was stable and not likely to cause corneal changes during the course of the study period)
- Active or recurrent ocular disease in either eye (eg, uveitis, ocular infection, chronic moderate to severe blepharitis or severe dry eye, ocular seasonal allergies) or sight-threatening disease (eg, neovascular age-related macular degeneration, diabetic macular edema) that, in the opinion of the investigator, could place the patient at a significant risk or interfere with the interpretation of the study data; patients with slowly progressive eye diseases (ie, mild cataracts, non-neovascular age-related macular degeneration) could be enrolled at the discretion of the investigator
- In the study eye, any history of external ocular or intraocular malignancy, and/or any history of benign ocular neoplasia that, in the investigator's opinion, resulted in clinically significant ocular morbidity
- History of herpetic ocular diseases (including herpes simplex virus and varicella zoster virus) in the study eye
- Bulbar conjunctival hyperemia on either macroscopic or slit-lamp examination of >+1 (mild) severity in either eye at baseline
- Active ocular surface findings other than bulbar conjunctival hyperemia, on either macroscopic or slit-lamp examination, of >+1 (mild) severity at baseline in the study eye
- History of moderate or worse (≥+2) bulbar conjunctival hyperemia due to marketed PGA use in either eye
- Anticipated wearing of contact lenses during the study in either eye, unless wear was temporarily discontinued before study visits, and before and after an administration day, according to the following: use of soft lenses was to be discontinued at least 3 days prior to baseline; use of rigid gas-permeable or hard contact lenses was to be discontinued at least 1 week prior to baseline; use of soft lenses was to be discontinued at least 3 days and use of rigid gas-permeable or hard contact lenses was to be discontinued at least 1 week prior to a scheduled study visit or administration day visit; use of contact lenses of any kind was prohibited within 1 week following any bimatoprost implant or sham administration
- Central corneal thickness of <480 or >620 µm in the study eye
- Anticipated need for any incisional or laser ocular surgery in either eye within the first 52 weeks of the study
- History of anatomically narrow angle that resulted in evidence of angle changes, or history of closed angle glaucoma in either eye (historically narrow-angled patients whose angle had been

opened by cataract surgery or peripheral iridotomy could have been eligible for enrollment if they had no evidence of angle abnormalities)
- History or evidence of a peripheral iridotomy/iridectomy in the inferior iris in the study eye
- History of trabeculectomy or other type of glaucoma surgery, including a glaucoma seton or aqueous bypass stent, in either eye
- History of laser trabeculoplasty within 6 months prior to screening in the study eye
- Peripheral anterior synechiae in the inferior iridocorneal angle on gonioscopic examination at screening in either eye (limited peripheral anterior synechiae resulting from previous laser trabeculoplasty in the fellow eye were not exclusionary)
- Visual field loss in either eye that, in the opinion of the investigator, was functionally significant (eg, split fixation, field defect within the central 10 degrees that was visually significant or likely to cause central visual impairment upon progression) or showed evidence of progression within the year prior to baseline (2 visual fields were required for qualification, 1 performed within the 10 months prior to or at screening, and 1 performed at baseline or during the washout period using the protocol-required testing method—the same testing methodology was to be used for all historical and study-related examinations for a given patient)
- Evidence of macular edema on screening OCT evaluation or in medical history in either eye
- Use of any ocular corticosteroids within 2 months prior to the baseline exam, or anticipated use during the study period in either eye, except for use of postoperative topical ocular corticosteroids from an administration day to day 7 following an administration, as described
- Anticipated use of other nonstudy topical ocular medications in either eye, except:
- Intermittent use of artificial tear products was allowed if not taken ≤15 minutes before any study procedure or ≤15 minutes before or after topical administration of study medication; intermittent use of ocular decongestants or antihistamines was allowed if not taken within 2 days prior to a scheduled visit and/or ≤15 minutes before or after topical administration of study medication; use of artificial tear products and ocular decongestants or antihistamines could be restarted 3 days after any bimatoprost implant or sham administration procedure
- Use of postoperative topical ocular antibiotics, corticosteroids, and NSAIDs from the administration day (day 1, week 16, and week 32) to day 7 following administration was allowed
- Use of systemic NSAIDs was permitted at any time
- Systemic medications containing beta-blockers were permitted, provided that the dose/dosing regimen had remained stable for at least 2 months prior to screening and was not anticipated to change during the duration of the study
- Therapy considered necessary for the patient's welfare could be given at the discretion of the investigator; if concurrent medications could have had an effect on study outcomes, these medications should have been administered in dosages that remained constant throughout the entire duration of the study

AS-OCT anterior segment optical coherence tomography, *BCVA* best-corrected visual acuity, *CECD* corneal endothelial cell density, *CRC* central reading center, *IOP* intraocular pressure, *NSAID* nonsteroidal anti-inflammatory drug, *OAG* open-angle glaucoma (ie, primary, pseudoexfoliation, or pigmentary glaucoma), *OCT* optical coherence tomography, *OHT* ocular hypertension, *PGA* prostaglandin analog

*Prior to a study protocol amendment in March 2017, study eye iridocorneal angle qualification was determined from AS-OCT images using a proprietary measurement as read by the CRC. The protocol was later amended to use the more clinically relevant methodology of assessment by clinical gonioscopy