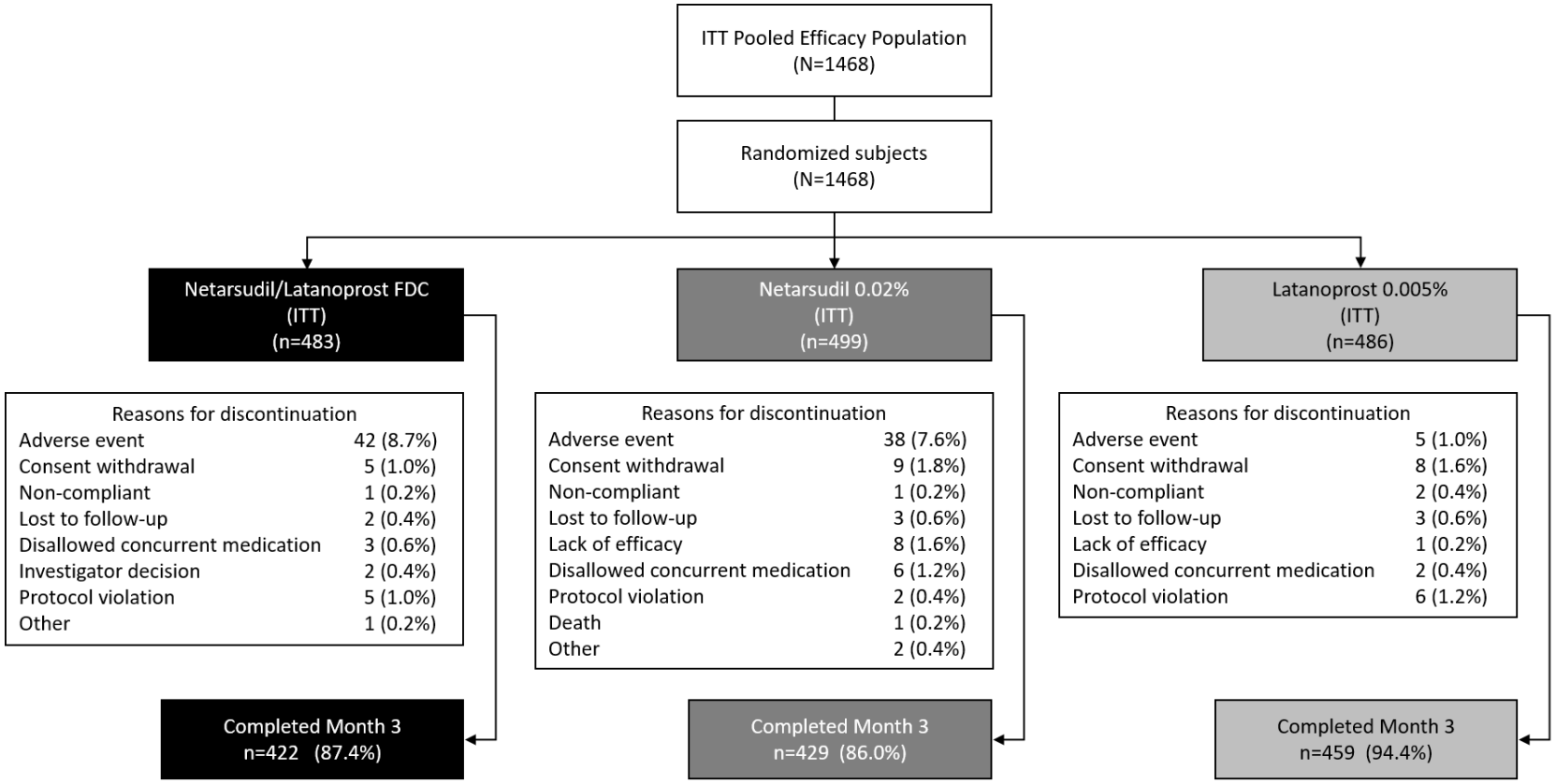
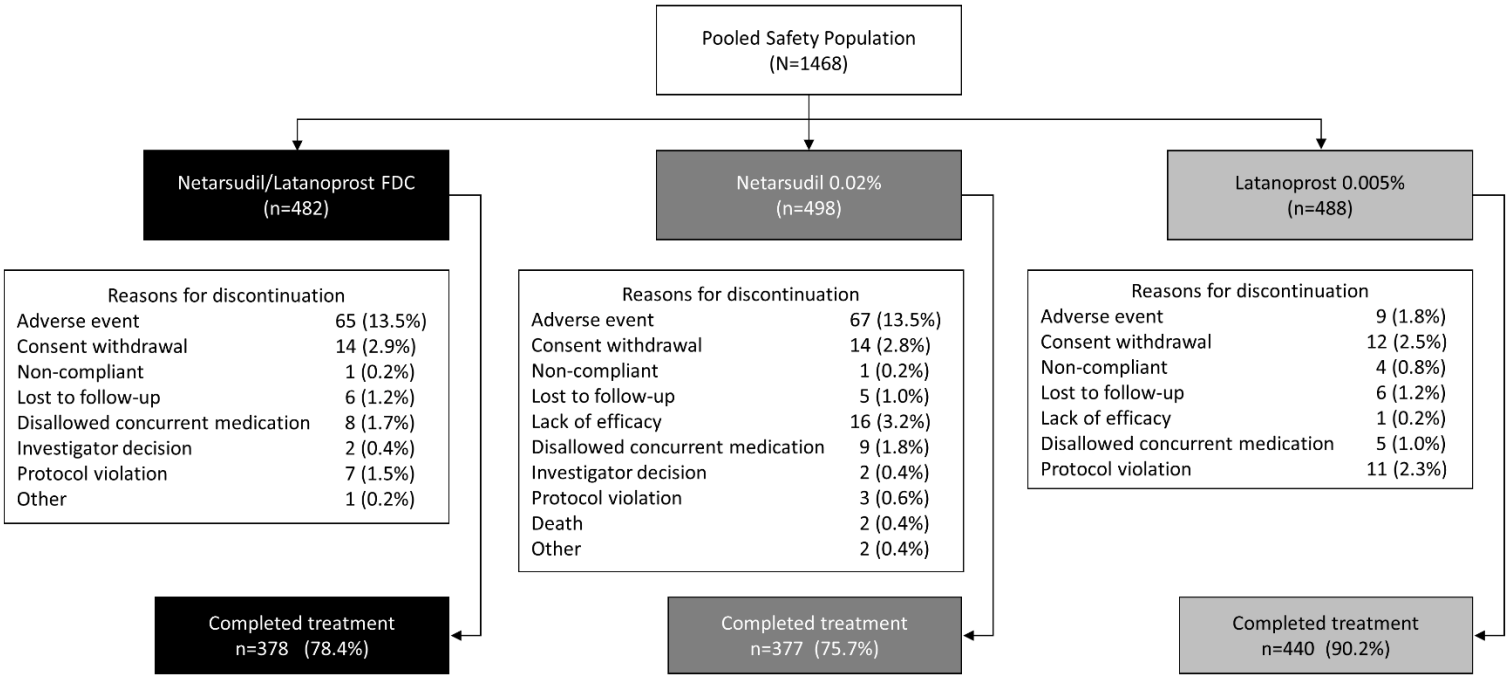
Supplementary Appendix

Figure S1. Patient Disposition in the Efficacy Population (to Month 3)



ITT, intent to treat

Figure S2. Patient Disposition in the Safety Population (to Month 12)



In MERCURY-1 one patient was randomized to netarsudil but received latanoprost thus the netarsudil group had 1 fewer patient, and the latanoprost group had 1 additional patient in their respective safety populations. In MERCURY-2 one patient was randomized to the to netarsudil/latanoprost FDC but received latanoprost, thus the netarsudil/latanoprost FDC had 1 fewer patient, and the latanoprost had 1 additional patient in their respective safety populations. Therefore, for the pooled safety population, compared with the efficacy population, there was 1 fewer patient each in the netarsudil/latanoprost FDC and netarsudil groups and 2 more patients in the latanoprost group.

Appendix Table S1. Inclusion and Exclusion Criteria

Inclusion criteria	
1	Must be 18 years of age or older (19 years of age or older in Canada)
2	Diagnosis of OAG or OHT in both eyes (OAG in one eye and OHT in the fellow eye was acceptable)
3	Unmedicated (post-washout) IOP >20 mmHg and <36 mmHg in both eyes at 2 qualification visits at 08:00 hours, 2–7 days apart. At the second qualification visit, IOP >17 mmHg and <36 mmHg in both eyes at 10:00 and 16:00 hours. Both eyes had to have qualified at all qualification visit time points
4	Best corrected visual acuity (BCVA) + 1.0 logMAR or better by ETDRS (equivalent to 20/200 or better Snellen visual acuity in each eye)
5	Be able and willing to give signed informed consent and follow study instructions
Ophthalmic exclusion criteria	
1	Clinically significant ocular disease (e.g., corneal edema, uveitis, severe keratoconjunctivitis sicca) which might have interfered with interpretation of the study efficacy endpoints or with safety assessments, including patients with glaucomatous damage so severe that washout of ocular hypotensive medications (if needed) for 1 month was judged unsafe as it would put the patient at risk for further vision loss
2	Pseudoexfoliation or pigment dispersion component glaucoma, history of angle closure glaucoma, or narrow angles (i.e., Grade 2 or less [Shaffer scale]; extreme narrow angle with complete or partial closure). Note: Prior laser peripheral iridotomy was NOT acceptable
3	Intraocular pressure ≥36 mmHg (unmedicated) in either eye at any time point (individuals who were excluded for this criterion were not allowed to attempt requalification) or use of more than 2 ocular hypotensive medications within 30 days of screening. Note: Fixed-dose combination medications, for the purpose of this exclusion criterion, was counted as 1 medication
4	Known hypersensitivity to any component of the formulation, to latanoprost, or to topical anesthetic
5	Previous glaucoma intraocular surgery, including SLT or ALT in either eye
6	Refractive surgery in either eye (e.g., radial keratotomy, PRK, LASIK, corneal cross-linking, etc.)
7	Ocular trauma in either eye within the 6 months prior to screening, or ocular surgery or non-refractive laser treatment within the 3 months prior to screening
8	Recent or current evidence of ocular infection or inflammation in either eye. Current evidence of clinically significant blepharitis, keratitis, or conjunctivitis. Additionally, current evidence or history of herpes simplex or zoster keratitis in either eye at screening was excluded
9	Use of ocular medication in either eye of any kind within 30 days of screening and throughout the study, with the exception of a) ocular hypotensive medications (which must have been washed out according to the provided schedule), b) lid scrubs (which may have been used prior to, but not after screening), c) lubricating drops for dry eye (which may have been used throughout the study), or d) non-corticosteroid or non-vasoconstrictor-containing allergy drops and allergy drops that do not have a redness reliever effect as prescribed by the Investigator

10	Mean central corneal thickness >620 µm in either eye at screening
11	Any abnormality preventing reliable applanation tonometry of either eye (e.g., keratoconus, etc.)
Systemic exclusion criteria	
12	Clinically significant abnormalities in laboratory tests at screening
13	Clinically significant systemic disease (e.g., uncontrolled diabetes, myasthenia gravis, hepatic, renal, endocrine or cardiovascular disorders) which might have interfered with the study
14	Participation in any investigational study within 60 days prior to screening [Netarsudil 0.02% and Latanoprost 0.005% Ophthalmic Solution Clinical Study Report: PG324-CS301 Aerie Pharmaceuticals, Inc. Confidential Page 29 of 141]
15	Systemic medication that could have had a substantial effect on IOP within 30 days prior to screening, or anticipated during the study, including any corticosteroid-containing containing drug regardless of route of administration
16	Women of childbearing potential who were pregnant, nursing, planning a pregnancy, or not using a medically acceptable form of birth control. An adult woman was considered to be of childbearing potential unless she was 1 year post-menopausal or 3 months post-surgical sterilization. All females of childbearing potential had to have a negative urine pregnancy test result at the screening examination and must not have intended to become pregnant during the study

ALT; argon laser trabeculoplasty; ETDRS, Early Treatment Diabetic Retinopathy Study; LASIK, laser-assisted *in situ* keratomileusis; OAG, open angle glaucoma; OHT, ocular hypertension; PRK, photo-refractive keratectomy; SLT, selective laser trabeculoplasty.

Appendix Table S2. Non-Ocular AEs Occurring at an Incidence of ≥1% in Any Treatment Group

	Netarsudil /Latanoprost n=482	Netarsudil n=498	Latanoprost n=488
Patients With any AE, n (%)	368 (76.3)	351 (70.5)	237 (48.6)
Infections and Infestations, n (%)	34 (7.1)	38 (7.6)	33 (6.8)
Upper respiratory tract infection	4 (0.8)	6 (1.2)	6 (1.2)
Bronchitis	4 (0.8)	6 (1.2)	5 (1.0)
Nasopharyngitis	8 (1.7)	5 (1.0)	2 (0.4)
Conjunctivitis[a]	4 (0.8)	6 (1.2)	1 (0.2)
Sinusitis	2 (0.4)	6 (1.2)	3 (0.6)
Influenza	0	2 (0.4)	6 (1.2)
Investigations, n (%)	28 (5.8)	38 (7.6)	26 (5.3)
Vital dye staining cornea present	18 (3.7)	21 (4.2)	10 (2.0)
Blood triglycerides increased	2 (0.4)	5 (1.0)	5 (1.0)
Blood glucose increased	4 (0.8)	5 (1.0)	1 (0.2)
Nervous system disorders, n (%)	17 (3.5)	17 (3.4)	12 (2.5)
Headache	5 (1.0)	9 (1.8)	2 (0.4)
Visual field defect	5 (1.0)	3 (0.6)	2 (0.4)
Skin and subcutaneous disorders, n (%)	21 (4.4)	7 (1.4)	3 (0.6)
Dermatitis contact	7 (1.5)	3 (0.6)	1 (0.2)
Vascular disorders, n (%)	5 (1.0)	8 (1.6)	9 (1.8)
Hypertension	3 (0.6)	8 (1.6)	6 (1.2)

AE, adverse event.

In the System Organ Class or Preferred Term, n is the number of patients with at least one adverse event; % is based on the number of patients

(n) in each treatment group for the population being analyzed. When reporting incidence, a patient was only counted once if they ever experienced an event within the System Organ Class or individual Preferred Term. System Organ Class and Preferred Term are based on Version 19.0 of the MedDRA coding dictionary.

[a]Conjunctivitis is documented in both Table 3 (Summary of Ocular AEs Reported in ≥5% of Patients) and in the System Organ Class and Preferred Term category Infections and Infestations