Title	A Patient Experience Study with ABBV-444 for Symptom Relief and Tolerability
Date of Current Version of Protocol	02 February 2023
Sponsor (Responsible Party)	AbbVie

1.0 Synopsis

Title	A Patient Experience Study with ABBV-444 for Symptom Relief and Tolerability
Sponsor (Responsible Party)	AbbVie Inc
Rationale and Background	ABBV-444 [redacted] will be the asset used for this study to assess the patient experience. [redacted] • [redacted] • [redacted] [redacted] However, there is a gap in our knowledge as to the effect of new formulation, ABBV-444, on patient symptom relief and product tolerability. As PROs are recognized as important measures for clinicians and patients, it is necessary to conduct a Patient Experience Study for ABBV-444.
Research Question	What is the effect of ABBV-444 on patient symptom relief and product tolerability?
Objectives and Endpoints	**Primary Objective:** To assess whether ABBV-444 will reduce patient symptoms evaluated by the Ocular Surface Disease Index (OSDI) questionnaire. **Secondary Objective:** To describe the patient experience of ABBV-444 by Patient Eye Drop Experience Survey and effect of immediate symptom relief by the Current Symptom Survey **Primary Endpoints:** Change from baseline in OSDI score at Day 30. **Secondary Endpoints:** • Patient Eye Drop Experience scores at Day 30 • Change from baseline in symptom scores within 5 mins post administration of ABBV-444 **Exploratory Endpoints:** • Patient Eye Drop Experience scores at Day 14 • Change from baseline in OSDI score at Day 14

Study Design	**Overall Study Design:** A single center, open-label, single arm study (ABBV-444) enrolling approximately 40 patients. **Inclusion/Exclusion Criteria for study population:** Inclusion criteria are as follows; • Participant must be ≥ 18 years of age • Written informed consent and written documentation, in accordance with the relevant country and local privacy requirements, had been obtained prior to any study procedures • Had used artificial tears for dry eyes within the past year • Females of childbearing potential, with a negative pregnancy test result at Screening Visit; these patients must have been currently using a reliable form of birth control and have agreed to use a reliable form of birth control for the duration of the study • OSDI score of ≥ 18 and ≤ 65 (based upon a 0 to 100 scale) at Screening and Baseline Visits Three consecutive tear break-up time (TBUT) tests ≤ 10 seconds in at least 1 eye at Day –7 (screening) • Grade 1 to 4 (modified National Eye Institute [NEI] Grid, score range = 0 to 5) staining in at least 1 area of the cornea (5 areas examined) or conjunctiva (6 areas examined) that was related to dry eye in at least 1 eye at both at Screening and Baseline Visits • Was able/agreed to continue to wear existing current spectacle correction during the study period (if applicable) • Currently corrected distance visual acuity of at least 20/32 Snellen equivalent in each eye using the 3-meter LogMar chart, with existing spectacle correction (if necessary) at Screening Visit • If using any form of topical ophthalmic cyclosporine (i.e., RESTASIS®), lifitegrast 5% ophthalmic solution (Xiidra®), participants must be using the drops for ≥ 90 days prior to the Screening Visit and plan to continue without change for the duration of the study • Intraocular pressure (IOP) ≤ 21 mmHg in both eyes for patients with primary open-angle glaucoma or ocular hypertension (OHT). Patients with primary open-angle glaucoma or OHT were included provided they were on stable monotherapy bilaterally with IOP controlled (≤ 21 mmHg) in both eyes. Any topical IOP-lowering medications must have had a start date of ≥ 3 months prior to Screening Visit date and dosage that was not expected to change during the study.

	• Was able to follow study instructions and was likely to complete all required visits Exclusion criteria are as follows: • Have uncontrolled severe systemic disease that, in the assessment of the investigator, would put safety of the participant at risk through participation, or which would prevent or confound protocol-specified assessments (e.g., hypertension and diabetes, Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, immunodeficiency disease, etc.) • Known allergy or sensitivity to the study products or their components • Females who were pregnant, nursing, or planning a pregnancy • Females of childbearing potential and who were not using a reliable method of contraception • Current enrollment in an investigational drug or device study or participation in such a study within 30 days of entry into this study at Screening Visit • Schirmer Test (with anesthesia) ≤ 2 mm in either eye at Screening Visit • Patient anticipated contact lens wear during the study, or the patient had worn contact lenses in the last 3 months prior to Screening Visit • Any scheduled or planned elective ocular or systemic surgery or procedure during the study, which in the investigator's opinion, may have impacted the patient's study participation • At the Screening and Baseline visits, either eye has corneal staining score of 5 in any of the 5 zones or a total score of > 19 based on the modified NEI grading scheme (score range = 0 to 5; graded in 5 zones of the cornea for a total score range of 0 to 25) or conjunctival staining score of 5 in any of the 6 zones based on the modified NEI grading scheme (score range = 0 to 5 per zone) • Use of systemic medications (over-the-counter, herbal, prescription, or nutritional supplements for dry eyes), which may have affected tear film or vision (including but not limited to the following: flax seed oil, fish oil, omega-3 supplements, cyclosporine, antihistamines, cholinergic agents, anticholinergics, antimuscarines, beta-blocking agents, tricyclic antidepressants, phenothiazines, estrogen-progesterone, and other estrogen derivatives), unless that medication had been used at the same dose for at least 3 months prior to screening and the dosage was not expected to change during the course of the study

	• Presence of 1 or more of the following ocular conditions in at least 1 eye:
	  • Active ocular infection or non-keratoconjunctivitis sicca (KCS) ocular inflammation
	  • Active ocular allergy
	• History of recurrent herpes keratitis or active disease within 6 months prior to Screening Visit
	• Corneal disorder or abnormality that affected corneal sensitivity or normal spreading of the tear film (except superficial punctate keratitis)
	• Severe blepharitis or obvious inflammation of the lid margin, which in the judgment of the investigator, may have interfered with the interpretation of the study results
	• Keratoconjunctivitis sicca secondary to the destruction of conjunctival goblet cells, such as occurs with vitamin A deficiency or scarring such as that with cicatricial pemphigoid, alkali burns, Stevens-Johnson syndrome, trachoma, or irradiation
	• Substantial non-KCS keratitis with overlying corneal stain or other significant corneal findings not directly related to dry eye; in addition, patients with dry eye signs/symptoms (e.g., filamentary keratitis) of a severity where topical monotherapy with an artificial tear would have been inappropriate
	• Occlusion of the lacrimal puncta for either eye, with punctal plugs or cauterization < 3 months prior to Screening Visit
	• History of prior ocular/ophthalmic surgery or trauma, which could affect corneal sensitivity and/or tear distribution (e.g., cataract surgery, laser-assisted in situ keratomileusis [LASIK], photorefractive keratectomy, or any surgery involving a limbal or corneal incision) within 6 months prior to at Screening Visit
	• Patients who were currently using topical ocular medication or had used topical ocular medication within 2 weeks of Screening Visit; however, patients who were being treated bilaterally with the following could have been considered:
	  • Current use of a marketed artificial tear, which was to have been discontinued at the Screening visit
	  • Monotherapy for glaucoma or OHT using a prostaglandin analog, beta-blocker, alpha-2 agonist, or carbonic anhydrase inhibitors; any topical IOP-lowering medications must have had a start date of ≥ 3 months prior to Screening Visit and the dosage was not expected to change during the study

	• If using any form of topical ophthalmic cyclosporine (i.e., RESTASIS®), lifitegrast 5% ophthalmic solution (Xiidra®), for less than 90 days prior to Screening Visit Patients who were currently being treated with both IOP-lowering medication and any form of topical ophthalmic cyclosporine (i.e., RESTASIS®) or lifitegrast 5% ophthalmic solution (Xiidra®) or generic of these medications cannot be enrolled • Patient had a condition or is in a situation, which in the investigator's opinion, may have put the patient at significant risk, may have confounded the study results, or may have interfered significantly with the patient's participation in the study
Sample size and Justification	This study is a descriptive non-hypothesis based study. 40 subjects will be enrolled in this study. Assuming a non-response rate of 10% at 30 days, there would be about 36 evaluable subjects.
Statistical methods	Analysis of all data will be descriptive. Biometrical analysis will be conducted based on subject demographics. Arithmetic mean, median, standard deviation (SD), standard error of the mean (SEM), interquartiles, minimum, and maximum will be used for the description of the data. Descriptive p-values (paired t-test) will be calculated for changes during the observation period, if adequate.

2.0 Abbreviations

AE	Adverse Event
PRN	As Needed
VAS	Visual Analog Scale
NA	Not Applicable
OTC	Over the Counter
PRO	Patient Reported Outcomes
OSDI	Ocular Surface Disease Index
PRK	Photorefractive Keratectomy
DED	Dry Eye Disease
IRB	Institutional Review Board
BID	Twice a Day
ICF	Informed Consent Form
AP	Analysis Population
OHT	Ocular Hypertension
IOP	Intraocular Pressure
NEI	National Eye Institute
LASIK	Laser-Assisted in Situ Keratomileusis
ICH	International Congress of Harmonization
GCP	Good Clinical Practice
GEP	Good Epidemiology Practice
CA	Competent Authority
EC	Ethics Committee
SAE	Serious Adverse Event
SOC	Standard of Care
PRO	Patient Reported Outcome
QoL	Quality of Life
SD	Standard Deviation
SEM	Standard Error of the Mean
EU	European Union

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4.0 Background and Rationale

4.1 Background

Dry eye disease (DED) is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles (Craig 2017).

To date, management and treatment of DED remains a large unmet medical need. Current mainstays include use of artificial tears and in more severe cases, tear retention (temporarily or permanently plugging the tear ducts) and anti-inflammatory therapies (Craig 2017). Artificial tears have been used for relief for symptoms of eye dryness (burning, irritation, and discomfort) and have proven to be safe and effective for lubricating and protecting the ocular surface from further irritation and relieving eye dryness symptoms.

[redacted]

There is a gap in our knowledge as to the effect of ABBV-444 on patient symptom relief, product tolerability and the patient eye drop experience. ABBV-444 is developed to meet the requirements of section 505G of the Federal Food, Drug and Cosmetic (FD&C) Act, including the over-the-counter (OTC) drug monograph and other applicable requirements, therefore ABBV-444 can be brought to market in the US via the OTC drug monograph

process. The OTC drug monograph process does not require a manufacturer to submit clinical trial data demonstrating safety and effectiveness of an individual drug, nor does it require an OTC drug to be approved by FDA prior to marketing.

[redacted]

5.0 Research Question, Objectives and Endpoints

5.1 Research Question

There is no formal hypothesis as the nature of this study is to describe the effect of ABBV-444 on symptoms relief of dry eye, such as burning, irritation and, discomfort due to eye dryness, the onset of action of relief and the patient experience across various timepoints. [redacted]

5.2 Study Objectives

Evaluate the effect of ABBV-444 on symptom relief, product tolerability and the patient experience after product use over time in adult patients with dry eye (patients with symptoms of burning, irritation, discomfort due to eye dryness).

5.2.1 Primary Objective

The primary objective is to assess whether ABBV-444 will reduce patient symptoms when evaluated by OSDI questionnaire.

5.2.2 Secondary Objectives

The secondary objective is to investigate the patient eye drop experience of ABBV-444 and the eye drop onset of action using a VAS-Current Symptom Survey.

5.3 Study Endpoints

5.3.1 Primary Endpoint

The primary endpoint is the change from baseline in OSDI score at Day 30.

5.3.2 Secondary Endpoints

- Patient Eye Drop Experience scores at Day 30
- Change from baseline in symptom scores within 5 mins post administration of ABBV-444

5.3.3 Exploratory Endpoints

- Patient Eye Drop Experience scores at Day 14
- Change from baseline in of OSDI score at Day 14

6.0 Study Design

6.1 Overall Design

This prospective, minimally interventional study will aim to describe the effect of ABBV-444 on relieving dry eye symptoms, such as burning, irritation, discomfort due to eye dryness (via the OSDI scoring tool), the patient experience (via a Patient Eye Drop Experience Survey) and the onset of action of the eye drop (via the Current Symptom Survey) across various timepoints (Figure 1). This will be an open-label, 1-arm study in which eye drops will be administered bilaterally as needed but minimally twice a day. Approximately 40 patients are planned to be enrolled at 1 site. A screening period of up to 6 days will be conducted prior to the Baseline Visit. Patients will be instructed to not administer any drops at least 4 hours prior to Baseline Visit. There will be three surveys administered to the subjects throughout the course of the study at the following timepoints:

1. OSDI will be given at Screening Visit, Baseline, Day 14 and Day 30/Early exit; and
2. Patient Eye Drop Experience Survey at Day 14 and Day 30/Early exit; and
3. Current Symptom Survey at Day 1; T0 (pre-dosing), T30s, T1min, T3min and T5min post-dose.
4. Study Product Usage Questionnaire at Day 14 and Day 30/Early exitStudy treatment is 30 days where OSDI scores, Patient Eye Drop Experience Survey scores and Current Symptom Survey scores will be obtained at the time points listed above. To assess product usage and compliance, the Study Product Usage Questionnaire will be administered at the time points listed above. Data will be collected via a paper questionnaire, sent to Lumanity where outcomes will be computed as mean changes from their baseline values.

Figure 1. Study Schematic

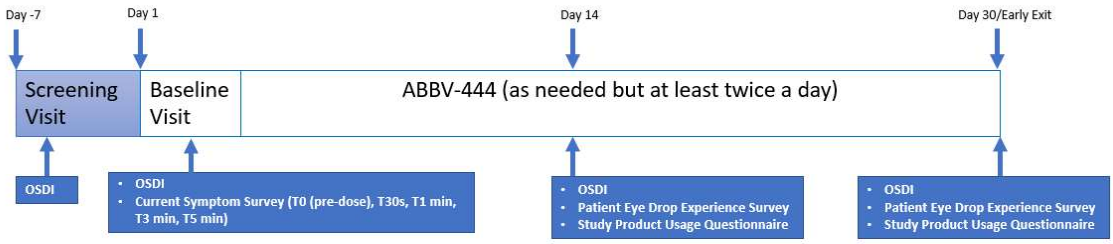


Table 1. Study Activities

It is recommended these procedures are completed in order listed at each study visit.

Study Visit	Screening (Day –7)	Baseline (Day 1)	Day 14	Day 30/Early Exit
Visit Window	(–7 to –1 days)		(+/– 3 days)	(+/– 3 days)
Written informed consent	X			
Urine pregnancy test (for females of childbearing potential only)	X			
Demography	X			
Adverse Event Assessment	X	X	X	X
Study Product Usage Questionnaire			X	X
OSDI Questionnaire	X	X	X	X
Biomicroscopy	X	X		
Tear Breakup Time (with fluorescein)	X			
Corneal staining (modified NEI grading scheme, with fluorescein)	X	X		
Conjunctival staining (modified NEI grading scheme, with lissamine green)	X	X		
Schirmer Test	X			
Intraocular Pressure (Goldmann Applanation tonometer)[a]	X			X
ABBV-444 dispensed		X	X	
Current Symptom Survey[b]		X		
Patient Eye Drop Experience Survey			X	X
Used and unused ABBV-444 returned				X

a. For patients with primary open-angle glaucoma or ocular hypertension only

b. Conducted at T0 (pre-dosing), T30 sec, T1min, T3 min and T5 min post-dose.

6.2 Study Population

The study population will consist of adult subjects with signs and symptoms of dry eye. The study will include 40 subjects with objective and subjective evidence of dry eye.

6.2.1 Inclusion Criteria

Patients that meet the following eligibility criteria will be included:

- Participant must be ≥ 18 years of age
- Written informed consent and written documentation, in accordance with the relevant country and local privacy requirements, had been obtained prior to any study procedures
- Had used artificial tears for dry eyes within the past year
- Females of childbearing potential, with a negative pregnancy test result at Screening; these patients must have been currently using a reliable form of birth control and have agreed to use a reliable form of birth control for the duration of the study
- OSDI score of ≥ 18 and ≤ 65 (based upon a 0 to 100 scale) at Screening and Baseline Visits
- Three consecutive tear break-up time (TBUT) tests ≤ 10 seconds in at least 1 eye at Screening Visit
- Grade 1 to 4 (modified National Eye Institute [NEI] Grid, score range = 0 to 5) staining in at least 1 area of the cornea (5 areas examined) or conjunctiva (6 areas examined) that was related to dry eye in at least 1 eye at both at Screening and Baseline Visits
- Was able/agreed to continue to wear existing current spectacle correction during the study period (if applicable)
- Currently corrected distance visual acuity of at least 20/32 Snellen equivalent in each eye using the 3-meter LogMar chart, with existing spectacle correction (if necessary) at Screening Visit
- If using any form of topical ophthalmic cyclosporine (i.e., RESTASIS®), lifitegrast 5% ophthalmic solution (Xiidra®), participants must be using the drops for ≥ 90 days prior to the Screening Visit and plan to continue without change for the duration of the study
- Intraocular pressure (IOP) ≤ 21 mmHg in both eyes at Screening Visit for patients with primary open-angle glaucoma or ocular hypertension (OHT). Patients with primary open-angle glaucoma or OHT were included provided

they were on stable monotherapy bilaterally with IOP controlled (≤ 21 mmHg) in both eyes. Any topical IOP-lowering medications must have had a start date of ≥ 3 months prior to Screening Visit date and dosage that was not expected to change during the study.

- Was able to follow study instructions and was likely to complete all required visits

6.2.2 Exclusion Criteria

Patients that have any of the following criteria will be excluded:

- Have uncontrolled severe systemic disease that, in the assessment of the investigator, would put safety of the participant at risk through participation, or which would prevent or confound protocol-specified assessments (e.g., hypertension and diabetes, Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, immunodeficiency disease, etc.)
- Known allergy or sensitivity to the study products or their components
- Females who were pregnant, nursing, or planning a pregnancy
- Females of childbearing potential and who were not using a reliable method of contraception
- Current enrollment in an investigational drug or device study or participation in such a study within 30 days of entry into this study at Screening Visit
- Schirmer Test (with anesthesia) ≤ 2 mm in either eye at Screening Visit
- Patient anticipated contact lens wear during the study, or the patient had worn contact lenses in the last 3 months prior to Screening Visit
- Any scheduled or planned elective ocular or systemic surgery or procedure during the study, which in the investigator's opinion, may have impacted the patient's study participation
- At the Screening and Baseline visits, either eye has corneal staining score of 5 in any of the 5 zones or a total score of > 19 based on the modified NEI grading scheme (score range = 0 to 5; graded in 5 zones of the cornea for a total score range of 0 to 25) or conjunctival staining score of 5 in any of the

6 zones based on the modified NEI grading scheme (score range = 0 to 5 per zone)

- Use of systemic medications (over-the-counter, herbal, prescription, or nutritional supplements for dry eyes), which may have affected tear film or vision (including but not limited to the following: flax seed oil, fish oil, omega-3 supplements, cyclosporine, antihistamines, cholinergic agents, anticholinergics, antimuscarines, beta-blocking agents, tricyclic antidepressants, phenothiazines, estrogen-progesterone, and other estrogen derivatives), unless that medication had been used at the same dose for at least 3 months prior to screening and the dosage was not expected to change during the course of the study
- Presence of 1 or more of the following ocular conditions in at least 1 eye:
  - Active ocular infection or non-keratoconjunctivitis sicca (KCS) ocular inflammation
  - Active ocular allergy
- History of recurrent herpes keratitis or active disease within 6 months prior to Screening Visit
- Corneal disorder or abnormality that affected corneal sensitivity or normal spreading of the tear film (except superficial punctate keratitis)
- Severe blepharitis or obvious inflammation of the lid margin, which in the judgment of the investigator, may have interfered with the interpretation of the study results
- Keratoconjunctivitis sicca secondary to the destruction of conjunctival goblet cells, such as occurs with vitamin A deficiency or scarring such as that with cicatricial pemphigoid, alkali burns, Stevens-Johnson syndrome, trachoma, or irradiation
- Substantial non-KCS keratitis with overlying corneal stain or other significant corneal findings not directly related to dry eye; in addition, patients with dry eye signs/symptoms (e.g., filamentary keratitis) of a severity where topical monotherapy with an artificial tear would have been inappropriate
- Occlusion of the lacrimal puncta for either eye, with punctal plugs or cauterization < 3 months prior to Screening Visit

- History of prior ocular/ophthalmic surgery or trauma, which could affect corneal sensitivity and/or tear distribution (e.g., cataract surgery, laser-assisted in situ keratomileusis [LASIK], photorefractive keratectomy, or any surgery involving a limbal or corneal incision) within 6 months prior to at Screening Visit
- Patients who were currently using topical ocular medication or had used topical ocular medication within 2 weeks of Screening Visit; however, patients who were being treated bilaterally with the following could have been considered:
  - Current use of a marketed artificial tear, which was to have been discontinued at the Screening Visit
  - Monotherapy for glaucoma or OHT using a prostaglandin analog, beta-blocker, alpha-2 agonist, or carbonic anhydrase inhibitors; any topical IOP-lowering medications must have had a start date of ≥ 3 months prior to Screening Visit and the dosage was not expected to change during the study
  - If using any form of topical ophthalmic cyclosporine (i.e., RESTASIS®), lifitegrast 5% ophthalmic solution (Xiidra®), for less than 90 days prior to Screening Visit
- Patients who were currently being treated with both IOP-lowering medication and any form of topical ophthalmic cyclosporine (i.e., RESTASIS®) or lifitegrast 5% ophthalmic solution (Xiidra®) or generic of these medications cannot be enrolled
- Patient had a condition or is in a situation, which in the investigator's opinion, may have put the patient at significant risk, may have confounded the study results, or may have interfered significantly with the patient's participation in the study

6.3 Data Management

6.3.1 Data Source

- OSDI is a validated PRO tool which consists of 12-item questionnaire evaluating a patient's dry eye symptom severity using a 6-point scale. All

participants will complete an OSDI Questionnaire. The purpose of this assessment is to capture a range of ocular surface symptoms, including symptoms related to dry eye, their severity, and their impact on the participant's ability to function, scaled into a 0 (no disease) to 100 (maximum severity of disease) score. Participants will complete the OSDI at Screening Visit, Baseline Visit, Day 14 and Day 30/Early exit.

- Patient Eye Drop Experience Survey will evaluate the short- and long-term subjective eye drop experience in relief and tolerability with the study eye drops using a VAS. All participants will complete the Patient Eye Drop Experience Survey Day 14 and Day 30/Early exit. Participants should be instructed to mark a vertical line on the anchored VAS that best describes their agreement with the statements within the questionnaire. The vendor Lumanity will then convert the participant's response to a numerical value (0 to 100). This is an overall evaluation, not per eye.

  Current Symptom Survey will evaluate the subjective onset of action of the eye drop as it pertains to relief and tolerability using a VAS. All participants will complete the Current Symptom Survey at Day 1. Survey will be administered at T0 (pre-dosing), T30s, T1min, T3min and T5min post-dosing. Participants should be instructed to mark a vertical line on the anchored VAS that best describes their agreement with the statements within the questionnaire. The vendor Lumanity will convert the participant's response to a numerical value (0 to 100). This is an overall evaluation, not per eye. Study Product Usage Questionnaire will evaluate the product usage and compliance of study drug. All participants will complete the Study Product Usage Questionnaire at Day 14 and Day 30/Early exit. The vendor Lumanity will collect the data.

6.3.2 Data Elements to Be Obtained

6.3.2.1 Prospective Data Component

OSDI

The OSDI will be administered to patients at Screening Visit, Baseline Visit, Day 14 and Day 30/Early exitpost-ABBV-444 administration. The OSDI can be found in Appendix C.

Patient Eye Drop Experience Survey

The Patient Eye Drop Experience Survey will be administered to patients at Day 14 and Day 30/Early exit, post ABBV-444 administration. The Patient Experience Survey can be found in Appendix D.

Current Symptom Survey

Current Symptom Survey will be administered to patients on Day 1; T0 (pre-dosing), T30s, T1min, T3min and T5 min post-dose at the study site. The Current Symptom Survey can be found in Appendix E.

Study Product Usage Questionnaire

Study Product Usage Questionnaire will be administered to patients at Day 14 and Day 30/Early exit. The Study Product Usage Questionnaire answers will be recorded in the Data Collection Forms, Appendix B.

6.3.3 Data Collection Methods

Eligible participants will be provided an IRB approved ICF. The physician or their staff will record any relevant patient information per standard of care (SOC) into their local patient health record keeping system. Patient eligibility, required demographics and additional visit information will be recorded in supplied paper study data forms (Appendix B). In addition, any applicable safety reporting will be recorded on the

supplied paper AE/SAE forms (Appendix F) and follow the process outlined in Section 9.3.

Paper English versions of the OSDI, Current Symptom Survey, Patient Eye Drop Experience Survey and the Study Product Usage Questionnaire will be provided to the site and labeled with a unique patient number for completion by the patient. Consented patients who meet all inclusion and none of the exclusion criteria will be allowed to complete these questionnaires at the specified study days. The participating site will be asked to send the completed questionnaires regularly to Lumanity (see Appendix A).

6.4 Treatments

6.4.1 Treatments Administered

During the treatment phase, each patient will be instructed to instill 1 to 2 drops of ABBV-444 in each eye, as needed, but at least 2 times daily. The same vial can be used for both eyes and should be used one time only. The used vial should then be stored in the supplied collection bag and returned to the site at the next scheduled visit for drug accountability, Section 6.4.5.

Patients are to be instructed during Screening Visit to not use any eye drops (artificial tears or prescription) for at least 4 hours prior to their Baseline Visit. If the patient is concurrently using allowed RESTASIS or IOP-lowering therapy drops during the study treatment they are to be instructed to wait a minimum of 15 minutes between administration of study drug and the allowed concomitant eye drops.

Table 2. Identity of Investigational Product

Investigational Product	ABBV-444
Mode/Route of Administration	Ophthalmic
Dosage Form	Solution, Single Dose Vial
Strength	Carboxymethylcellulose Sodium [redacted] and Glycerin [redacted] Ophthalmic Solution Preservative Free with Potassium Chloride [redacted]
Frequency of Administration	Minimally BID
Storage Conditions	Between 15°C and 30°C (59 – 86°F)

Packaging and Labeling

ABBV-444 will be packaged in vial/carton/resealable pouch with quantities sufficient to accommodate study design. Each vial/carton/resealable pouch will be labeled per local regulatory requirements. The labels must remain affixed to the vial/carton/resealable pouches. All blank spaces should be completed by site staff before dispensing to subject.

6.4.2 Storage and Disposition of Study Drug

ABBV-444 must be stored as described in table above. The investigational products are for investigational use only and are to be used only within the context of this study. The study drugs supplied for this study must be maintained under adequate security and stored under the conditions specified on the respective drugs' label until dispensed for subject use or destroyed on site as appropriate.

6.4.3 Selection and Timing of Dose for Each Patient

ABBV-444 will be self-administered bilaterally at minimum twice a day (BID) Day 1 through Day 30/Early exit. A single dose vial will be used to administer the eye drops. One single dose vial should be used bilaterally, for both eyes. If the patient feels it necessary to obtain better relief, ABBV-444 can be administered as needed (PRN) bilaterally.

6.4.4 Study Drug Usage for Each Patient

The 2-question Study Eye Drop Usage Questionnaire will be completed by each patient at Day 14 and Day 30/Early exit to capture the date and time of their last study drug administration and their overall compliance to study drug usage.

Question 1: "What date and time did you last use your study eye drops?"

Question 2: "On average, how many times did you administer the eye drops per day?"

Sites should review each patient's response to ensure that the last administration of their study drug was ≥ 4 hours from the start of completing this questionnaire and that they are using their study eye drops at minimum 2 times per day. Should either of the patient's responses be out of compliance, the site should discuss with the patient to ensure they dose correctly from that point forward.

6.4.5 Study Drug Accountability

The investigator or his representative will verify that study drug supplies are received intact and in the correct amounts. This will be documented by signing and dating the Proof of Receipt or similar document. The investigator or his designated representatives will dispense study drug only to patients enrolled in the study. A current (running) and accurate inventory of study drug will be kept by the investigator and will include shipping invoices and the date on which study drug is allocated to patients, as well as used and unused study drug returned by patients. An overall accountability of the study drug will be performed and verified by the investigator or his representative throughout the study until its completion. Upon completion or termination of the study, all original containers (containing used and unused study drug) will be destroyed on site per instructions supplied by AbbVie. All study drug accountability logs will be sent to Lumanity, per contact information found in Appendix A.

7.0 Statistical Methods, Sample Size and Analysis Plan

Analysis of all data will be descriptive. Biometrical analysis will be conducted based on subject demographics. Arithmetic mean, median, standard deviation (SD), standard error of the mean (SEM), interquartiles, minimum, and maximum will be used for the description of the data. Descriptive p-values (paired t-test) will be calculated for changes during the observation period, if adequate.

7.1 Analysis Populations

The full analysis set (FAS) will consist of all subjects who are study eligible based on the inclusion and exclusion criteria and complete 30 days of treatment for this study.

7.2 Sample Size and Justification

This study is not a confirmatory study with hypothesis testing. At least 40 subjects will be enrolled in this study based on a feasibility assessment. Assuming a non-response rate of 10% at Day 30, there would be about 36 evaluable subjects.

7.3 Statistical Analysis Plan

7.3.1 General Approach

Demographic and other baseline subject characteristics will be summarized. Descriptive statistics (such as mean, standard deviation, median, minimum and maximum) will be presented for each continuous variable. Categorical variables will be displayed using frequency counts and percentages.**Patients Demographics, Disease Characteristics, Treatment Patterns, and Treatment Discontinuation**

Demographics and other baseline characteristics of the study subjects will be summarized descriptive statistics (such as mean, median, standard deviation, median, standard error of the mean (SEM) interquartiles, min and max) will be presented for each continuous variable, Categorical variables will displayed using frequency counts with percentages.

7.3.3 Primary Analysis

The analysis is based on full analysis set (FAS). The primary endpoint is the change of OSDI score from baseline at Day 30. The change of OSDI score will be summarized using descriptive statistics: mean, median, standard deviation, standard error of the mean (SEM), interquartiles, min and max. A descriptive p-value (paired t-test) will be calculated for the change of OSDI score if the data is adequate.

7.3.4 Secondary Analysis

The secondary endpoints of interest are the Patient Eye Drop Experience Survey score at Day 30 and the change of Current Symptom Survey score from baseline at T5min post-dose. The score of each item in the Patient Eye Drop Experience Survey at Day 30 and the change of Current Symptom Survey at T5min will be summarized using descriptive statistics: mean, median, standard deviation, standard error of the mean (SEM), interquartiles, min and max. In the meanwhile, one bar plot for the mean of the score with 95% confidence interval will be made for each of the secondary endpoints. The change of Current Symptom Survey score from baseline at T5min will be summarized using the same descriptive statistics. A descriptive p-value (paired t-test) will be calculated for the change of VAS score if the data is adequate.

7.3.5 Exploratory Analysis

The exploratory endpoints of interest are the Patient Eye Drop Experience Survey score at Day 14 and the change of OSDI score from baseline at Day 14. The score of each item in the Patient Eye Drop Experience Survey at Day 14 and the change of OSDI score from baseline at Day 14 will be summarized using descriptive statistics: mean, median, standard deviation, standard error of the mean (SEM), interquartiles, min and max. In the meanwhile, one bar plot for the mean of the score with 95% confidence interval will be made for each of the exploratory endpoints. The change of OSDI from baseline at Day 14 will be summarized using the same descriptive statistics. A descriptive p-value (paired t-test) will be calculated for the change of VAS score if the data is adequate.

8.0 Study Conduct

8.1 Responsibilities Within the Study

The study will be conducted by the Investigator and Lumanity under AbbVie oversight. The study shall be conducted as described in the approved protocol.

8.2 Protection of Human Subjects

The study will be conducted in accordance with ethical principles that have their origin in the current Declaration of Helsinki and will follow the principles of International Conference Harmonization Good Clinical Practice (ICH GCP) and Good Epidemiology Practice (GEP) and applicable regulatory requirements. IRB/EC notification or approval will be obtained prior to the initiation of the study as necessary per local Regulation.

8.3 Patient Information/Informed Consent

This study will be run in compliance with local laws and regulations. Notification/submission to the responsible Ethics Committee, and/or Competent Authorities will be performed as required by local laws and regulations (see Country Information page [Appendix A]).

Written informed consent will be obtained prior to patient inclusion.

9.0 Safety Reporting

Please notify AbbVie of any adverse event whether serious or nonserious and record the information in the provided AE/SAE Data Collection Form (Appendix F).

The AbbVie contact details are specified in Country Information page (Appendix A).

The following adverse event and safety information definitions and further information is provided should you need to report any safety information to AbbVie.

9.1 Adverse Event Definition

An AE is defined as any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in the protocol or labeling, as well as from "special situations" as accidental or intentional overdose, medication error, occupational or accidental exposure, off-label use, drug abuse, drug misuse, or drug withdrawal, all which must be reported whether associated with an adverse event or not. Any worsening of a pre-existing condition or illness is considered an AE and should be reported as a new AE.

9.2 Serious Adverse Event Definition

If an adverse event meets any of the following criteria, it is considered a serious adverse event (SAE):

Death of Patient	An event that results in the death of a patient.
Life-Threatening	An event that, in the opinion of the treating physician, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form.
Hospitalization or Prolongation of Hospitalization	An event that results in an admission to the hospital for any length of time or prolongs the patient's hospital stay. This does not include an emergency room visit or admission to an outpatient facility.
Congenital Anomaly	An anomaly detected at or after birth or any anomaly that result in fetal loss.

Persistent or Significant Disability/Incapacity	An event that results in a condition that substantially interferes with the activities of daily living of a patient. Disability is not intended to include experiences of relatively minor medical significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).
Important Medical Event Requiring Medical or Surgical Intervention to Prevent Serious Outcome	An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may jeopardize the patient and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of patient, life threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Additionally, any elective or spontaneous abortion or stillbirth is considered an important medical event. Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

9.3 Serious and Nonserious Adverse Event Reporting

- For **serious adverse events** from patients using an AbbVie product – notify AbbVie within 24 hours of the physician becoming aware of the event.
- For **nonserious adverse events** from patients using an AbbVie product – notify AbbVie within 15 calendar days of the physician becoming aware of the event, including "special situations."

AbbVie contact details are specified in the Country Information page (Appendix A).

9.4 Patient Reported Outcomes and/or Quality of Life Questionnaires

Patient Reported Outcome (PRO) or Quality of Life (QoL) questionnaires data are not considered a potential source of adverse events for the purposes of this study. However,

the physician should review the PRO or questionnaire(s) data. If the physician identifies an adverse event and it is determined to be related to an AbbVie authorized product, report to AbbVie as described above and to the relevant Regulatory Authority, as required by local laws and regulations.

10.0 Pregnancy

If at any time you need to report a pregnancy occurrence in a patient taking an AbbVie product, the physician can notify AbbVie using the contact details in Appendix A within 24 hours of the physician becoming aware of the pregnancy.

Pregnancy is not considered an adverse event. The medical outcome for either mother or infant, meeting any serious criteria including an elective or spontaneous abortion, is considered a serious adverse event and must be reported to AbbVie using the details in Appendix A within 24 hours of the site becoming aware of the event and to the relevant Regulatory Authority, as required by local laws and regulations.

11.0 Product Complaint

Product complaints will be collected as part of this study; if at any time you need to report a Product Complaint (Appendix G) please refer to this section for the definition and reporting requirements.

11.1 Definition

A Product Complaint is any Complaint related to the biologic or drug component of the product or to the medical device component(s).

For a product this may include, but is not limited to, damaged/broken product or packaging, product appearance whose color/markings do not match the labeling, labeling discrepancies/inadequacies in the labeling/instructions (example: printing illegible), missing components/product, device not working properly, or packaging issues.

For medical devices, a product complaint also includes all deaths of a patient using the device, any illness, injury, or adverse event in the proximity of the device, an adverse event that could be a result of using the device, any event needing medical or surgical intervention including hospitalization while using the device and use errors.

Any information available to help in the determination of causality by the device to the events outlined directly above should be reported.

11.2 Complaint Reporting

Product complaints concerning an AbbVie authorized product must be reported to AbbVie within 24 hours of the site's knowledge of the event using the contact details in Appendix A. All follow-up information is to be reported to the Sponsor (or an authorized representative) and documented in source as required by the Sponsor. All complaints will be monitored on an ongoing basis.

Product Complaints may require return of the product with the alleged complaint condition (syringe, pen, etc.). In instances where a return is requested, every effort should be made by the physician to return the product within 30 days. If returns cannot be accommodated within 30 days, the site will need to provide justification and an estimated date of return.

The description of the complaint is important for AbbVie in order to enable AbbVie to investigate and determine if any corrective actions are required.

12.0 Privacy and Confidentiality

12.1 Data De-Identification

Before Personal Data is shared with AbbVie, the institution/doctor and his/her staff must replace any information that could directly identify a patient (such as name, address, and contact information) with a generic code which AbbVie cannot link to patient identity. Personal Data with identifying information may not be shared.

12.2 Data Storage and Access

AbbVie will store study data and any Coded Data it receives in a limited-access, secure storage space. AbbVie may retain the study data and any Coded Data reported to it for as long as AbbVie is conducting medical research in the therapeutic area that is the subject of this research or as long as the marketed product related to this research project is used, or longer, if required by EU or local laws and regulations governing research activities.

12.3 Reports and Publications

At the end of the study, a report or publication will be written by AbbVie. This report/publication will contain a description of the objectives of the study, the methodology and its results and conclusions. The completed questionnaires and the final study output are the confidential property of AbbVie and may not be released to unauthorized people in any form (publications or presentations) without the express written approval from AbbVie.

13.0 References

1. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Executive Summary. Ocul Surf. 2017;15:575-628.
2. Miller KL, Walt JG, Mink DR, et al. Minimal clinically important difference for the ocular surface disease index. Arch Ophthalmol. 2010;128(1):94-101.

14.0 Appendices

Appendix A. Study or Country Information Page

A Patient Experience Study with ABBV-444 for Symptom Relief and Tolerability

Name of Medical Director: [redacted] PhD
Address: 2525 Dupont Drive, Irvine, CA, 92612
Country: United States
Phone: [redacted]
Email: [redacted]

Safety/Pregnancy Reporting to:

E-mail: IR-Clinical-SAE@abbvie.com
Fax: [redacted]
Back-up fax number: [redacted]

Complaints Reporting to:

E-mail: Productqualitycomplaints@abbvie.com

Shipment address for Study Data Forms /Questionnaires:

Name: Lumanity
Address: 200 Pine Ave, Suite 200, Long Beach, CA 90802
Country: USA
Phone: [redacted]
Fax: [redacted]

Requirements per Local Regulations:

Competent Authority approval ☐

Competent Authority notification ☐

Competent Authority involvement not required ☒

Ethics Committee approval ☒

Ethics Committee notification ☐

Ethics Committee involvement not required ☐

Written Patient Informed Consent required: ☐ No* ☒ Yes

*Provide a reason_____

Regulatory requirements, other (if applicable):

Name of Affiliate Medical Director or equivalent role (i.e., Regulatory for US)

Signature Date

Appendix B. Study Data Collection Forms

Date (MM/DD/YYYY): _____

Patient Identification Number: _____

Eligibility

Did the patient meet all the Inclusion Criteria in Protocol Section 6.2.1? ☐Yes ☐No

If "No", which criteria were not met:_____

Did the patient meet any Exclusion Criteria in Protocol Section 6.2.2? ☐Yes ☐No

If "No", which criteria were met: _____

Patient Demographics

Age: _____
Sex: ☐ Female ☐ Male
Race: ☐ American Indian or Alaska Native ☐ Asian
☐ Black or African American ☐ White ☐ Other
Ethnicity: ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Study Visits

Screening Date: (MM/DD/YYYY): _____

Baseline/Day 1: (MM/DD/YYYY): _____

1. If applicable, did you use your RESTASIS or IOP-lowering therapy drops in the past 4 hours? ☐Yes ☐No ☐NA

Day 14: (MM/DD/YYYY): _____

2. What date and time did you last use your study eye drops? _____

3. On average, how many times did you administer the eye drops per day? _____

Day 30: (MM/DD/YYYY): _____

1. What date and time did you last use your study eye drops? _____

2. On average, how many times did you administer the eye drops per day? _____

Safety

Were there any AE/SAEs Reported? ☐Yes ☐No
If "Yes", complete appropriate form(s) in Appendix F.

_____ _____
Principle Investigator Date

Appendix C. Ocular Surface Disease Index (OSDI)

Ocular Surface Disease Index© (OSDI©)[2]

Ask your patient the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING DURING THE LAST WEEK :

	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

HAVE PROBLEMS WITH YOUR EYES LIMITED YOU IN PERFORMING ANY OF THE FOLLOWING DURING THE LAST WEEK :

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

HAVE YOUR EYES FELT UNCOMFORTABLE
IN ANY OF THE FOLLOWING SITUATIONS DURING THE LAST WEEK :

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

ADD SUBTOTALS A, B, AND C TO OBTAIN D
(D = SUM OF SCORES FOR ALL QUESTIONS ANSWERED) (D)

TOTAL NUMBER OF QUESTIONS ANSWERED
(DO NOT INCLUDE QUESTIONS ANSWERED N/A) (E)

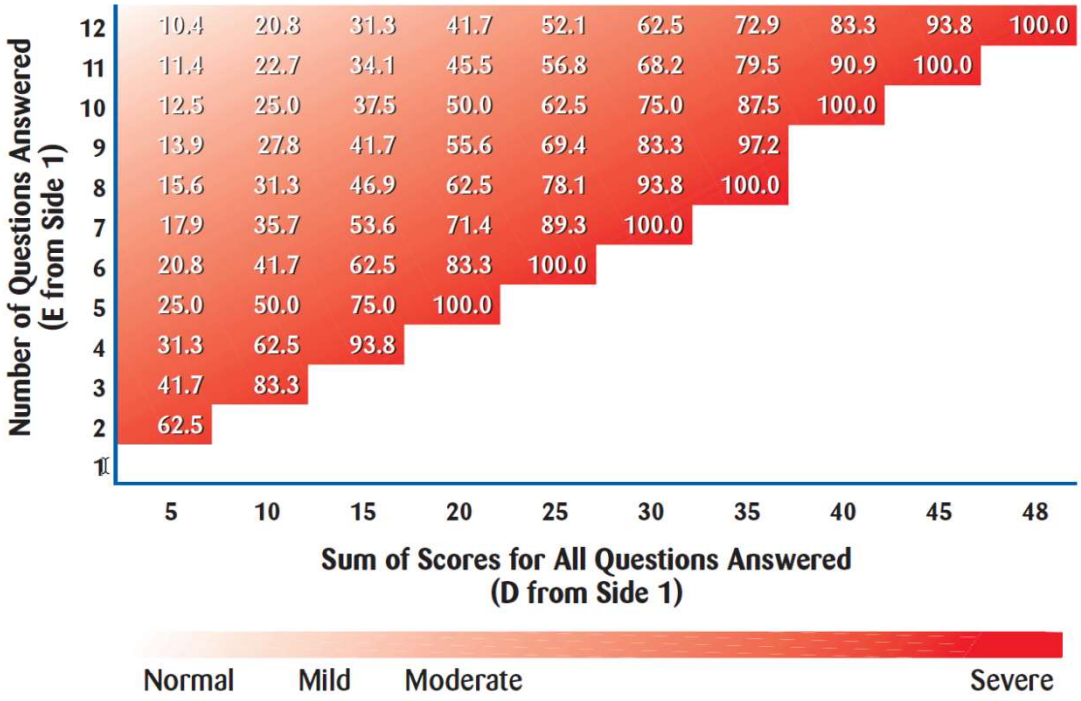
Please turn over the questionnaire to calculate the patient's final OSDI© score.

Evaluating the OSDI© Score[1]

The OSDI© is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI© is a valid and reliable instrument for measuring dry eye disease severity (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient's Dry Eye Disease[1,2]

Use your answers D and E from Side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.*
Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.



*Values to determine dry eye disease severity calculated using the OSDI© formula:
OSDI© = (sum of scores) x 25 / (# of questions answered)

Patient's Name: _____ **Date:** _____

How long has the patient experienced dry eye? _____

Eye Care Professional's Comments: _____

Tear and place in patient's chart for follow-up care on next visit.

Reference: 1. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000;118:615-621. **2.** Data on file, Allergan, Inc.

ALLERGAN INSPIRE PHARMACEUTICALS, INC.

 Re-order: 4941843

Appendix D. ABBV-444 Patient Eye Drop Experience Survey

This questionnaire evaluates the short-and long-term subjective experience in comfort and vision with the study eye drops, as well as the tolerability of the assigned study eye drops over the past week, using a VAS. At Day 14 and Day 30/Early exit visits, the Study Eye Drop Experience and Tolerability Survey will be completed by each participant. Participants should be instructed to mark a vertical line on the anchored VAS that best describes their agreement with the statements within the questionnaire. A trained member of the study site personnel will then use the provided VAS ruler to convert the participant's response to a numerical value (0 to 100). This is an overall evaluation, not per eye. The questionnaire will read as follows (Note: The VAS scales will be actual scales and not just text as indicated below for the purposes of this protocol.):

Think about your experience with the study eye drops within the first 5 minutes of applying them. Using the scales provided below, please mark a vertical line at the place that best describes your agreement with the following statements:

1. The study eye drops do not cause stinging or burning in my eyes. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

2. The study eye drops provided immediate relief of my eye dryness upon instillation. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

3. The study eye drops immediately soothed my eye dryness upon instillation (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

4. I did not experience much blurry or fluctuating vision after instillation of the study eye drops (VAS anchors: 0 = A lot of blur, 100 = Low blur)

A lot of blur ——————————————— Low Blur

5. The study eye drop provided immediate comfort to my eye dryness upon instillation. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

Now think about your experience with the study eye drops 30 minutes after you applied them. Using the scales provided below, please mark a vertical line at the place that best describes your agreement with the following statements:

6. The study eye drops are very soothing for my eye dryness. (VAS anchors: 0 = strongly disagree,
100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

7. The study eye drops did not feel sticky. (VAS anchors: 0 = strongly disagree,
100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

8. The study eye drops continued to provide relief of my eye discomfort. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

9.The study eye drop continued to provide comfort to my eye dryness. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

Now think about your experience with the study eye drops over the last 24 hours after you applied them. Using the scales provided below, please mark a vertical line at the place that best describes your agreement with the following statements:

10. The study eye drops provided relief day and night to my eye dryness (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

11.The study eye drop provided comfort to my eye dryness day and night. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

Lastly, think about how you have felt over the last 5 days while using the study eye drops. Using the scales provided below, please mark a vertical line at the place that best describes your agreement with the following statements:

12. The study eye drops provided lasting relief of my eye dryness. (VAS anchors: 0 = strongly disagree, 100 = strongly agree)

Strongly Disagree ——————————————— Strongly Agree

13. These eye drops have provided relief during conditions that lead to eye dryness due to; use of a fan, a heater, in a dry environment, digital device use, reading a book and/or watching TV (VAS anchors: 0 = strongly disagree, 100 = strongly agree, N/A)

Strongly Disagree ——————————————— Strongly Agree

Appendix E. Current Symptom Survey

At Day 1: T0 (pre-dose), 30 secs post-dose, 1 min post-dose, 3 min post-dose, 5 min post-dose:

Current Symptom Survey will be completed by each patient to measure their ocular symptoms at current moment. Patients should be instructed to mark a vertical line on the anchored VAS that best captures how their eyes are feeling at the current moment. A trained member of the study personnel will then use the provided ruler to convert the patient's response to a numerical value (0 to 100). This is an overall evaluation, not per eye. The questionnaire will read as follows (note: the VAS scales will be an actual scale and not just text as indicated below for the purposes of this protocol).

Think about how your eyes are feeling right now. Then, using the scales provided below, please mark a vertical line that best describes your experience with these symptoms:

1. Burning/stinging due to dryness of the eye (VAS anchors: 0 = no burning/stinging, 100 = maximum burning/stinging)

Strongly Disagree ——————————————— Strongly Agree

2. Grittiness/foreign body sensation due to dryness of the eye (VAS anchors: 0 = no grittiness/foreign body sensation, 100 = maximum grittiness/foreign body sensation)

Strongly Disagree ——————————————— Strongly Agree

3. Eye Dryness (VAS anchors: 0 = no dryness, 100 = maximum dryness)

Strongly Disagree ——————————————— Strongly Agree

4. Blurry/fluctuating vision due to dryness of the eye (VAS anchors: 0 = no blurry/fluctuating vision, 100 = maximum blurry/fluctuating vision)

Strongly Disagree ——————————————— Strongly Agree

5. Overall discomfort due to dryness of the eye (VAS anchors: 0 = no pain/discomfort, 100 = maximum pain/discomfort)

Strongly Disagree ——————————————— Strongly Agree

Appendix F. AE/SAE Collection Form

Case ID # (for AbbVie internal use only)	

Please send this form to PPDINDPharmacovigilance@abbvie.com as soon as the event occurs.

STUDY INFORMATION

Study Name:	**Protocol Number:**
Date of this report (DDMONYYYY)	

PATIENT INFORMATION

Patient Information:	**Patient ID:**
Date of Birth (DDMONYYYY/MONYYYY):	**Patient Name or Initials:**
Gender (at birth): ☐ **M** ☐ **F**	**Patient Ethnicity:**

ABBVIE PRODUCT INFORMATION (***Note:*** Copy this page to add more products.)

Product Name	**Start Date** (DDMONYYYY)	**Stop Date** (if	**Status**	**Indication**	**Dose/ Frequen**	**Expirati on Date**
1)			☐ Ongoing ☐ Interrupted ☐ Withdrawn ☐ Not applicable			
2)			☐ Ongoing ☐ Interrupted ☐ Withdrawn ☐ Not applicable			

Lot # ***(relevant to event)***	If Lot Number is Unknown or Unavailable, check ONE box below to explain the reason.
1)	☐ Reporter does not have the lot #. Provide rationale*:_____ _____ ☐ Reporter declined to provide lot # ☐ Reporter contact for lot # was unsuccessful. ☐ Reporter's contact information was not available.
2)	☐ Reporter does not have the lot #. Provide rationale*: _____ _____

Product Name	Start Date (DDMONYYYY)	Stop Date (if	Status	Indication	Dose/ Frequen	Expirati on Date
	☐ Reporter declined to provide lot #			☐ Reporter contact for lot # was unsuccessful.		
	☐ Reporter's contact information was not available.					

***If unable to provide Lot number, provide rationale in the field above: discarded, not accessible to physician, not on patient's file, did not receive in original package, not legible on package.**

ADVERSE EVENT (AE)INFORMATION (*Including Special Situations with/without AE such us pregnancy; and Product Complaints)*

Adverse Event Term	Event Onset Date (DDMONYYYY)	Event End Date (DDMONYYYY)	Outcome	Seriousness	Causality
			☐ Fatal ☐ Recovered ☐ Unknown ☐ Recovering ☐ Not Recovered ☐ Recovered w/Sequelae	Serious ☐ Death ☐ Hospitalization/Prolonged hospitalization ☐ Congenial anomaly ☐ Life Threatening ☐ Medically Important ☐ Persistent of Significant Disability ☐ Non serious	☐ Related ☐ Not Related ☐ Not Reported
			☐ Fatal ☐ Recovered ☐ Unknown ☐ Recovering ☐ Not Recovered ☐ Recovered w/Sequelae	Serious ☐ Death ☐ Hospitalization/Prolonged hospitalization ☐ Congenial anomaly ☐ Life Threatening ☐ Medically Important ☐ Persistent of Significant Disability ☐ Non serious	☐ Related ☐ Not Related ☐ Not Reported

ADVERSE EVENT(S) DESCRIPTION (Describe complementary information (symptoms, intensity, chronology, etc):

CONCOMITANT DRUGS (***Note:*** Copy this page to add more medications)

Were any Concomitant Drugs Taken?	☐ Yes	☐ No

Concomitant Drug	Start Date (DDMONYYYY)	End Date (DDMONYYYY)	Dose	Route	Indication

TREATMENT DRUGS

Treatment Drug	Start Date (DDMONYYYY)	End Date (DDMONYYYY)	Dose	Route	Indication

DIAGNOSTICS AND TEST RESULTS

Test name	Test Date (DDMONYYYY)	Results)	Unit(s)	Normal range

MEDICAL HISTORY (***Note:*** Copy this page to add more medical history terms)

Was there a relevant Medical History?		☐ Yes ☐ No
Medical History Term (including medical, surgical, smoking & alcohol)	**Onset Date** (DDMONYYYY)	**End Date** / ongoing(DDMONYYYY)

Was there a relevant Medical History?		☐ Yes ☐ No
Medical History Term (including medical, surgical, smoking & alcohol)	**Onset Date** (DDMONYYYY)	**End Date** / Ongoing(DDMONYYYY)

ALLERGIES TO MEDICATION

Medication Allergies (describe below)

PHYSICIAN INFORMATION

Physician Name:	**E-mail:**	**Phone No:**
Street Address:	**City:**	**State/Territory:**
Postcode:	**Country:**	
Date:	**Signature:**	

Appendix G. Product Complaint Form

Please fill out this Product Complaint Form and send it to the following email address: RD_PQC_QA@abbvie.com

GENERAL INFORMATION		
Is an emergency resupply required? ☐ YES ☐ NO **If yes, please inform your AbbVie monitor or CRA immediately.**		
Study Number:		
Investigator/Site information Name: _____ Address: _____ Country: _____		
Site Number/RIC Number:		
1	Site Awareness Date :	
2	Date complaint reported to AbbVie:	
3	Date of occurrence/onset (When did this happen):	
4	Describe complaint: (Provide a detailed description of the complaint including what the subject was doing when the complaint occurred) _____ _____	
Details regarding the drug product/medical device		
5	Product Name:	
6	Serial/lot number of drug product or medical device:	
7	Kit number of drug product or medical device: (List all if more than one)	
8	Subject Number:	
9	Was the dose administered? (If YES, complete questions 10-14; if NO, proceed to question 15)	☐ No ☐ Yes
10	Dose administered (i.e. quantity, volume):	
11	Units of dose administered:	
12	**Who administered the medication?** ☐ Investigator ☐ Study Nurse ☐ Patient ☐ Other:	
13	Was the administration performed per protocol? (if NO, please explain)	☐ No ☐ Yes
14	Was the subject/caregiver trained? (If NO, please specify)	☐ No ☐ Yes
15	Were there administration problems prior to this event? (If YES, please specify)	☐ No ☐ Yes
16	Did interruption of study medication occur? (If YES, please specify)	☐ No ☐ Yes

Product Complaint

Details regarding the staff member reporting the complaint to enable AbbVie to follow-up and information gathering regarding complaint		
17	Role: ☐ Physician ☐ Nurse ☐ Pharmacy ☐ Hospital/institution ☐ Coordinator ☐ Other:	
18	Name:	
19	Site address:	
20	Work email address:	
21	Work phone number:	
Details regarding the complaint		
22	Were any tests done to verify condition? (If YES, specify)	☐ No ☐ Yes
23	Is the complaint drug product/medical device available and quarantined? (If NO, explain)	☐ No ☐ Yes
24	Can representative pictures be provided?	☐ No ☐ Yes
25	How many units with suspected issue? (i.e. 1 bottle, 10 tablets, 1 pump, 1 tube, etc.):	
26	Was medication shipment damaged? If YES, provide Clinical Supplies Shipping Request (CSSR).	☐ No ☐ Yes
27	Was the tamper evident seal of the kit intact when it arrived at the site?	☐ No ☐ Yes
28	Did the site personnel or subject notice any other unusual attributes with the kit/bottle/packaging? (If YES, specify)	☐ No ☐ Yes
29	Any additional comments regarding the complaint that are considered relevant and were not collected in any of the sections above?	
30	Was this complaint associated with an adverse event? If YES, adverse event serial number:	☐ No ☐ Yes

Title	A Patient Experience Study with ABBV-444 for Symptom Relief and Tolerability
Date of Version of Protocol	02 February 2023

Approved by:

[redacted]

Electronically signed by: [redacted]
Reason: Approver
Date: [redacted]

Protocol Author – [redacted] Date

[redacted]

Electronically signed by: [redacted]
Reason: Subject Matter Expert
Date: [redacted]

Scientific Director – [redacted] Date

[redacted]