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ORIGINAL RESEARCH

Qualitative Development of the Allergan Satisfaction with Treatment Experience Questionnaire (ASTEQ) Instrument, a Patient-Reported Outcome Measure in Glaucoma and Ocular Hypertension

Richard M. Evans · Martha Gauthier · Margot L. Goodkin · Joice T. Huang

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ABSTRACT

Introduction: Sustained-release intraocular implants provide a therapeutic option for open-angle glaucoma (OAG) and ocular hypertension (OHT) patients who are non-compliant with eyedrops. Currently, there are no published patient-reported outcome (PRO) measures that assess treatment satisfaction with intraocular implants. To address this gap, a new PRO instrument, the Allergan Satisfaction with Treatment Experience Questionnaire (ASTEQ), has been developed in accordance with Food and Drug Administration guidance.

Methods: Qualitative research interviews were conducted among patients with OAG/OHT who had received three intraocular injections of a sustained-release bimatoprost (10 or 15 μg) implant within the clinical trial setting. A preliminary conceptual framework capturing treatment satisfaction concepts in glaucoma, as identified from the literature, was used to develop a semi-structured interview guide. A concept elicitation (CE) interview to identify aspects of the glaucoma treatment experience pertinent to intraocular implants provided content for a draft instrument. A cognitive debriefing (CD) interview to test the instrument's interpretability, relevance, and validity informed its subsequent refinement. Interview analysis followed a grounded theory approach to identify data patterns and relationships.

Results: CE interviews (n = 19) indicated that participants' main considerations in rating satisfaction with implant treatment were physical comfort during preparation for the implant and implant administration, anxiety about the procedure, frequency of implant administration, possible side effects, convenience and accessibility of the implant, relationship with the clinician, and lifestyle fit. Draft ASTEQ revision based on CD interviews (n = 20) and readability tests yielded a nine-item ASTEQ instrument comprising satisfaction with overall implant experience and frequency of administration, occurrence/bother of immediate and long-term side effects, worry about implant administration and possible risks/side effects, and physical discomfort during preparation for the implant and implant administration.

Conclusion: The ASTEQ instrument has demonstrated content validity in patients with OAG/OHT treated with a sustained-release bimatoprost implant. Further research is necessary to evaluate its psychometric properties.

R. M. Evans
Medical Center Ophthalmology Associates, San Antonio, TX, USA

M. Gauthier
Lumanity, Boston, MA, USA

M. L. Goodkin · J. T. Huang (✉)
Allergan (an AbbVie company), 2525 Dupont Drive, Irvine, CA, USA
e-mail: Joice.Huang@AbbVie.com

Keywords: Allergan Satisfaction with Treatment Experience Questionnaire; Bimatoprost; Glaucoma; Instrument development; Intraocular implant; Ocular hypertension; Patient-reported outcome measures; Treatment satisfaction

Key Summary Points

Why carry out this study?

Intraocular implants present a novel therapeutic option for patients with glaucoma or ocular hypertension who have difficulty using eyedrops, but there is no existing patient-reported outcome (PRO) instrument to assess treatment satisfaction with intraocular implants.

To address this gap, a new PRO instrument, the Allergan Satisfaction with Treatment Experience Questionnaire (ASTEQ), has been developed in accordance with regulatory guidance on the development and evaluation of PRO measures for use in drug registration trials.

What was learned from the study?

Based on rigorous qualitative research analysis methods, this study provides evidence to support the content validity of the nine-item ASTEQ instrument in patients with open-angle glaucoma and ocular hypertension undergoing treatment with a sustained-release bimatoprost implant.

The ASTEQ instrument assesses concepts determined to be important and relevant to patients receiving intraocular implant therapy for open-angle glaucoma or ocular hypertension. Further research is required to evaluate the instrument's psychometric performance to support its use in clinical trials.

INTRODUCTION

Open-angle glaucoma, the predominant form of glaucoma in the Western world [1], is a chronic, progressive optic neuropathy characterized by retinal ganglion cell loss with associated visual field defects [2]. The global prevalence of open-angle glaucoma in the 40- to 80-year-old age group is estimated at 3.05%, with the elderly and those of African and Asian ancestry being disproportionately affected [1].

Elevated intraocular pressure (IOP) is the most important risk factor, and the only known modifiable one, for the development of open-angle glaucoma [3–5]. Lowering of IOP has been established to reduce the risk of glaucoma development and progression to vision loss at all levels of disease severity [6–10]. Standard first-line treatment for ocular hypertension and open-angle glaucoma comprises IOP-lowering eyedrops. However, delivery of drops into the eye can be problematic for patients, and compliance with daily eyedrop medication is often poor [11–13], particularly among older patients and the infirm [14]. Sustained-release implants may provide a solution for patients with glaucoma or ocular hypertension who have difficulty using eyedrops. Durysta® (Allergan, an AbbVie company, North Chicago, IL), a sustained-release bimatoprost intracameral implant consisting of 10 μg bimatoprost in a drug delivery system, was approved by the US Food and Drug Administration (FDA) in 2020 based on results of the two 20-month phase 3 ARTEMIS registration trials [15, 16].

A comprehensive review of the literature, reported here, has determined that there are no currently available patient-reported outcome (PRO) measures that assess treatment satisfaction with intraocular implants. This paper reports the qualitative research process used to design, in accordance with FDA guidance on development of clinical outcome assessments (COAs) [17, 18], a new PRO measure of treatment experience satisfaction relevant to intraocular implants for use in open-angle glaucoma or ocular hypertension.

METHODS

Literature Search and Gap Analysis

A comprehensive literature review was conducted to identify currently available PRO instruments assessing treatment satisfaction in patients with glaucoma. Ovid MEDLINE® and EMBASE® bibliographic databases were searched using keywords for (i) satisfaction, (ii) PRO measures, (iii) eye disease, and (iv) glaucoma. The Patient-Reported Outcome and Quality of Life Instruments (PROQOLID) database, and the Patient-Reported Outcomes and Drug Marketing Authorizations (PROLabels) database (a repository of PRO claims granted by the FDA or European Medicines Agency) were searched manually under the "eye diseases" category. Ovid MEDLINE® and EMBASE® searches were confined to English language articles published between 2009 and 2015. Relevant PRO instruments identified by in-depth review of full-length articles and labels selected by these searches were checked for their compliance with FDA guidance on PRO development at the time of the search (2015) [17].

PRO Instrument Development

Preliminary Conceptual Framework and Overall Development

Development of the new PRO instrument, the Allergan Satisfaction with Treatment Experience Questionnaire (ASTEQ), was guided by a series of qualitative research interviews conducted among individuals with open-angle glaucoma or ocular hypertension who had received treatment with a sustained-release bimatoprost intraocular implant within the clinical trial setting. A preliminary conceptual framework capturing treatment satisfaction concepts pertinent to glaucoma (as identified by the literature review) was used to develop a qualitative, semi-structured interview guide for the initial (concept elicitation) interview. The purpose of this interview was to uncover specific aspects of the glaucoma treatment experience that were most relevant and important to these patients. Results from the interview were used to draft a PRO instrument, which was later refined based on input from a subsequent (cognitive debriefing) interview undertaken to test the interpretability and relevance of the instrument. Independent review board approval was obtained for all study documents and protocols. All subjects provided their written informed consent to participate in the study, and written authorization to access personal health information in accordance with the US Health Insurance Portability and Accountability Act (HIPAA).

Patient Recruitment

Subjects with open-angle glaucoma or ocular hypertension were recruited from Allergan's phase 3 ARTEMIS 1 and ARTEMIS 2 clinical studies of a sustained-release bimatoprost implant in dose strengths of either 10 μg or 15 μg (ClinicalTrials.gov, identifiers NCT02247804 and NCT02250651) [15, 16]. In addition to meeting the ARTEMIS study eligibility criteria, participants were required to (i) have received three scheduled intraocular injections of the 10 μg or 15 μg sustained-release bimatoprost implant at 16-week intervals as part of the ARTEMIS study; (ii) be available to complete a 60-min interview between 2 and 16 weeks after the third implant administration; (iii) be able and willing to understand and follow study instructions and complete all required visits and procedures; and (iv) be fluent in English. Those with a history of alcohol/drug abuse in the past 12 months, or a medical condition that would prevent participation in a 60-min interview, were excluded.

Concept Elicitation Interviews

Concept elicitation interviews with study participants were conducted face-to-face or by telephone by trained personnel, using a semi-structured interview guide to probe and explore concepts associated with satisfaction with treatment experience in glaucoma and ocular hypertension through a series of open-ended questions. This approach was intended to reduce possible bias in soliciting responses, and to encourage participants to describe their experiences in their own words. Targeted

probing questions were asked to elicit additional information if patients did not provide spontaneous responses. Each interview was audio recorded and lasted approximately 60 min.

Audio recordings were transcribed verbatim and anonymized before analysis. Interview analysis followed a grounded theory approach involving an iterative process of constant comparison of transcripts to one another and to existing codes and categories for the purpose of identifying patterns and relationships in the data [19, 20]. An initial code list compiled from the literature review findings, preliminary conceptual framework, interview guide, and research objectives was used to catalogue concepts reported spontaneously or following probing by the interviewer. This code list was updated as necessary to reflect the actual terms participants used to describe concepts, and to incorporate newly emerging data. Codes were applied to specific text within each transcript and queried for frequency across transcripts by constant comparative method using ATLAS.ti version 7.5.18 qualitative data analysis software (Atlas.ti GmbH, Berlin).

The adequacy of the sample size was confirmed through concept saturation, which refers to the point at which further data collection ceases to generate any new or distinctive categories, high-level concepts, or substantive codes [19]. Concept saturation was assessed by documenting concept emergence across sets of successive interviews [21].

Concept Review and Item Generation

Following analysis of the concept elicitation interview, a series of three concept generation meetings was held to identify items for inclusion in the draft PRO instrument, based on prespecified criteria and FDA guidance recommendations [17]. Item selection was guided by the frequency with which a concept was mentioned, the applicability of the concept to all potential respondents, and clear attribution to treatment. The preliminary structure and format of the PRO instrument, order of items, response options, and recall period were determined, and a draft version of the ASTEQ instrument was developed.

Cognitive Debriefing Interviews

Cognitive debriefing interviews were conducted with a different sample of ARTEMIS 1 and 2 study participants; enrollment criteria for the cognitive debriefing interview were identical to those for the concept elicitation interview (as outlined in the Patient Recruitment section). The purpose of the cognitive debriefing interview was to assess how well study participants understood the instructions, items, and response options in the draft ASTEQ instrument; to determine whether its format and wording were appropriate; and to ensure that the instrument captured all concepts of importance and relevance to the study population. Given this objective, it was important that the cognitive debriefing interview should be conducted with a different sample of study participants to that used for the concept elicitation interview. To ensure a standardized interview technique, a Cognitive Interview Guide was developed, which included questions relating to content validity (how well the instrument captures participants' overall experiences), ease of completion, comprehensiveness and appropriateness of the format, response scales, and recall period, as well as specific concept probes to determine whether participants consider conceptually similar items to be the same or different. To reduce the possibility of introducing interviewer bias, participants were encouraged to verbalize their thoughts while completing the draft PRO instrument and to identify words, terms, or concepts that they did not understand. Where necessary, more specific verbal probing was used to ensure the objectives of the interview were accomplished. As with the concept elicitation interview, the cognitive debriefing interview lasted approximately 60 min, and was audio recorded, transcribed verbatim, and anonymized before analysis.

Analysis of cognitive debriefing interview data was likewise founded on a grounded theory approach [19, 20]. An initial coding scheme was developed from the Cognitive Interview Guide and research objectives, and updated as new themes emerged from the interviews. Analysis of coding data patterns and frequencies was conducted using ATLAS.ti version 7.5.18 software (Atlas.ti GmbH, Berlin).

PRO Instrument Revision

On completion of the cognitive debriefing interview, the draft PRO instrument was modified on the basis of participants' feedback and all revisions were documented. In line with FDA guidance on PRO development [17], the draft PRO instrument was evaluated item by item for appropriate readability, as determined using the new Dale–Chall readability formula (developed specifically for evaluating health education materials) [22] and the Flesch–Kincaid readability formula [23]. If it was judged that an item would present difficulty in comprehension to a sixth-grader (an 11- to 12-year-old), the wording was revised as appropriate for the intended patient population.

Conceptual Framework Revision

As recommended by FDA guidance on PRO development [18], the preliminary conceptual framework was updated to illustrate how patients' satisfaction with the intraocular implant treatment experience, as described during concept elicitation interviews and confirmed during cognitive interviews, mapped to the contents of the ASTEQ instrument.

RESULTS

Literature Search and Gap Analysis

A total of 281 articles describing patient satisfaction in glaucoma were identified from a targeted literature search across the four databases, of which three articles were selected for full-text review and concept extraction. From these final articles, three PRO instruments were selected for in-depth analysis: the Eye-Drop Satisfaction Questionnaire (EDSQ), a 21-item PRO developed in French and English in 2007 to measure patient satisfaction and compliance with eye-drop medication [24, 25], the Glaucoma Patient Satisfaction Questionnaire (Glausat), a 22-item PRO developed in Spanish in 2010 to evaluate patients' satisfaction with glaucoma treatment [26], and the Treatment Impact Patient Satisfaction Scale (TIPSS), a 45-item PRO developed in New Zealand in 2012 to assess patient satisfaction and treatment impact in subjects using topical IOP-lowering medication [27]. However, all three instruments were found to have limitations, including incomplete qualitative and/or psychometric assessment (Glausat, TIPPS), failure to meet all psychometric validation requirements (EDSQ), possible language bias (EDSQ, Glausat), and lack of published evidence to support the instrument's use in clinical trials or FDA/European Medicines Agency labeling claims (EDSQ, Glausat, TIPPS). For these reasons, it was decided that a new PRO instrument was necessary to assess treatment experience satisfaction in glaucoma.

A preliminary conceptual framework describing treatment experience satisfaction in patients with glaucoma was developed from five articles selected from the targeted literature search [24, 26–29]. Concepts collectively identified in these articles, amounting to 74 items spread across 13 domains, were incorporated into the preliminary conceptual framework (Table 1).

PRO Instrument Development

Concept Elicitation Interview Findings

Concept elicitation interviews were conducted among 19 study participants, all of whom had received treatment with one of the two dose strengths of the sustained-release bimatoprost intraocular implant during their participation in the ARTEMIS trials. Concept saturation findings indicated that this sample size was adequate. Interviewees ranged in age from 29 to 83 years, included similar numbers of males and females, were predominantly White (68.4%) and non-Hispanic/Latino (89.5%), and varied widely in educational level; most had used topical IOP-lowering medication prior to their enrollment in the study (84.2%) (Table 2).

Concepts of Treatment Satisfaction

When asked to describe which factors they considered when rating their satisfaction with implant treatment experience, participants most frequently mentioned "physical comfort during application of the implant" (n = 15, 78.9%), "feeling anxious about the procedure" (n = 15, 78.9%), "frequency of implant

Table 1 Preliminary conceptual framework for assessing patient satisfaction with treatment experience in glaucoma, based on the published literature (up to 2015) describing patient experience with topical ocular hypotensive medication

Concept	Domain	General concept
Burning/stinging	Adverse events	Bothersomeness with medication use
Grittiness/sandiness		
Dryness		
Unpleasant feelings		
Eye itching		
Blurred vision		
Uncomfortable tearing		
Tiredness		
Difficulty breathing		
Timing of medication use	Convenience of medication use	Satisfaction with treatment use
Frequency of medication use		
Convenience of bottle opening		
Convenience of drop dosing		
Convenience of checking amount of drops left in bottle		
Convenience of eyedrops as a treatment for glaucoma		
Overall satisfaction with eyedrops	Satisfaction with treatment	Treatment satisfaction
Eyedrops are the best option available		
Feel good about treatment		

Table 1 continued

Concept	Domain	General concept
Remembering to take medications	Adherence/Compliance	Treatment burden
Voluntary treatment break		
Forgetting treatment		
Intention to keep taking medication		
Accurately deliver drops in eye	Ease of use	
Deliver right amount of medication in eye		
Ease of head position		
Ease of reading label on bottle		
Ease of opening bottle		
Ease of medication use		
Routine		
Burden of treatment		
Difficulty in taking drops		
Multiplicity of treatment		
Physical difficulties (e.g., shaking, arthritis)		
Use of device to assist drop delivery		
Discomfort		
Worry about putting things in eye		
Blink reflex		
Difficulty remembering to take drops at right time		
Storage of eye drops in good condition		

Table 1 continued

Concept	Domain	General concept
Others' reaction to redness of eyes	Emotional impacts	Impacts of treatment
Self-conscious of redness of eyes		
Concern over eye appearance		
Confidence in the treatment		
Feeling about lifelong treatment		
Interference with quality of life	Quality of Life impacts	
Quality of life worsened		
Prevention of future vision problems	Improvement of visual symptoms	Effectiveness of medications
Prevention of current vision problems		
Treatment is good for me		
Drops allow me to control my glaucoma		
I did not get worse		
Satisfaction with quantity of information given on disease	Information received on disease and treatment	Patient–clinician relationship
Satisfaction with quantity of information given on treatment		
Frequency of information given on IOP		
Frequency of information given on visual field		
Training in drop instillation		
Visit frequency to clinician	Disease burden	
Satisfaction with visit frequency		
Satisfaction with clinician care		
Feedback and motivation		
Follow-up and motivation		

Table 1 continued

Concept	Domain	General concept
Sex	Sociodemographics	Patient characteristics
Age		
Marital status		
Level of education		
Self-administering or external help		
Previous experience with IOP/POAG among family or friends		
Professional status	Professional activities	
Number of working hours		
Daytime availability		
Frequency of long journeys		
Ease of prescription renewal when away		
Frequency of nights spent away from home	Travel	

IOP intraocular pressure; *POAG* primary open-angle glaucoma

Table 2 Baseline demographic and clinical characteristics of participants in the concept elicitation and cognitive debriefing interviews

Characteristic	Concept elicitation interview *n* = 19	Cognitive debriefing interview *n* = 20
Age, years		
Mean (SD)	60.7 (14.1)	59.5 (12.2)
Range	29–83	37–81
Sex, *n* (%)		
Female	10 (52.6)	8 (40.0)
Race, *n* (%)		
White	13 (68.4)	13 (65.0)
Black/African American	5 (26.3)	1 (5.0)
Other	1 (5.3)	6 (30.00
Ethnicity, *n* (%)		
Non-Hispanic/Latino	17 (89.5)	13 (65.0)
Hispanic/Latino	2 (10.5)	7 (35.0)
Educational level, *n* (%)		
Non-degree	8 (42.1)	9 (45.0)
Associate's/Bachelor's/Master's degree	9 (47.4)	11 (55.0)
Professional school degree	1 (5.3)	–
Doctoral degree	1 (5.3)	–
Employment status, *n* (%)		
Part/full-time work	10 (52.6)	10 (50.0)
Retired	8 (42.1)	9 (45.0)
Student	1 (5.3)	–
Homemaker	–	1 (5.0)
Diagnosis, *n* (%)		
Glaucoma	15 (78.9)	17 (85.0)
Ocular hypertension	4 (21.1)	3 (15.0)
Time since diagnosis, years		
Mean (SD)	5.6 (5.)	9.4 (10.0)
Range	0.8–17.1	1.1–34.0
Intraocular pressure, *n* (%)		
$\leq$ 25 mm Hg	12 (63.2)	12 (60.0)
$>$ 25 mm Hg	7 (36.8)	8 (40.0)

Table 2 continued

Characteristic	Concept elicitation interview*n* = 19	Cognitive debriefing interview*n* = 20
Medication history, *n* (%)		
No prior use	3 (15.8)	5 (25.0)
Recent use (within last 6–12 months)	1 (5.3)	3 (15.0)
Long-term use (≥ 6 months)	15 (78.9)	12 (60.0)

SD standard deviation

administration" (*n* = 13, 68.4%), "possible side effects of the implant" (*n* = 13, 68.4%), "convenience and accessibility of the implant" (*n* = 12, 63.2%), "relationship with the clinician" (*n* = 12, 63.2%), "degree to which the implant experience fits with my lifestyle" (*n* = 11, 57.9%), and "physical comfort during preparation for the implant procedure" (*n* = 10, 52.6%). Less frequently mentioned factors included: "ease of compliance," "feeling worried or scared about procedural mistakes or side effects," "impact on activities of daily living," "impact on work," "efficacy," "side effects related to antiseptic drops," "intention to use or continue," and "social impact," (Fig. 1).

With regard to physical comfort during implant administration, most participants reported both positive (no sensation) and negative (pain, pressure, or stinging sensation) experiences with needle insertion. Participants' anxiety about the procedure stemmed from concerns about their lack of understanding of the procedure and/or the prospect of receiving an injection in the eye. Most participants who mentioned anxiety about the procedure reported that they experienced less anxiety during the second and third implant administrations. Comments on the frequency of implant administration were generally positive, focusing on the advantages of treatment every 4 months rather than twice daily, although one participant stated that they would not want to repeat the implant procedure every 4 months. Participants reported fewer positive than negative experiences with side effects (the latter included instances of ocular soreness [*n* = 1], pain [*n* = 1], increased sensitivity [*n* = 2], puffiness [*n* = 1], dryness [*n* = 4], and redness [*n* = 6] that participants attributed to the implant experience). Most participants commented positively on implant convenience and accessibility, noting that the procedure was quick, completed within a reasonable timeframe, and had minimal impact on their day-to-day routine; a minority stated that appointments occasionally involved long wait times. Physical comfort during preparation for the implant procedure was generally described in negative terms, with participants specifically citing exposure to bright lights, use of eyelid retractors, and application of topical povidone iodine antiseptic as causes of discomfort; in contrast, two participants found the preparation procedure to involve no discomfort. Participants frequently reported a positive relationship with the clinician when describing their satisfaction with the implant administration experience, noting that medical staff were very good at alleviating procedure-related anxiety. While relationship with the clinician was not recommended as an item for inclusion in the final PRO instrument since it is not a concept that can be modified by treatment, it is nevertheless an important aspect of the implant treatment experience.

When asked to provide overall satisfaction ratings with each of the three implant administrations, a larger proportion of study participants reported being "mostly" or "very" satisfied with the third implant (*n* = 5, 100%) than with the first (*n* = 6, 66.6%) or second (*n* = 3, 42.9%) implants. Table 3 summarizes representative quotes volunteered by study participants when questioned on details of their satisfaction with

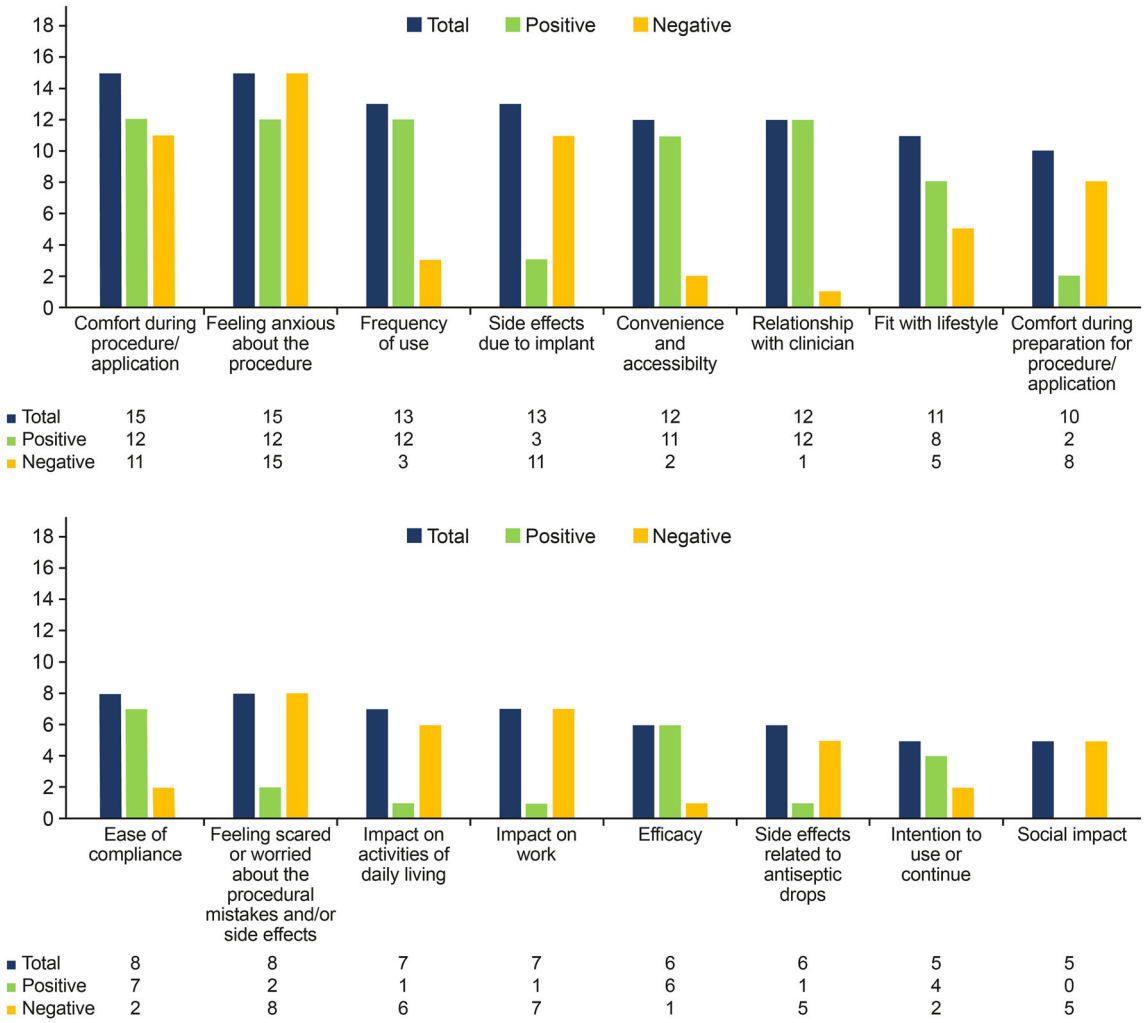

Fig. 1 Qualitative results of concept elicitation interviews: participants' most frequently reported considerations when rating treatment satisfaction. Tabulated data indicate numbers of participants reporting each item, and the directionality of response (positive or negative). Patients may report both positive and negative experiences; thus, the total number is not necessarily the sum of positives and negatives

the implant experience during the concept elicitation interviews.

Draft PRO Instrument

A draft version of the ASTEQ Implant Experience instrument was developed from qualitative analysis of the concept elicitation interview data. This version included 11 items: (1) satisfaction with the overall experience of receiving the implant, (2) satisfaction with the frequency of implant administration, (3) satisfaction with the convenience of receiving the implant, (4) satisfaction with how implant administration every 4 months fits with my routine or schedule, (5) satisfaction with the ease of following the implant treatment routine (e.g., remembering to schedule and attend the implant appointment), (6) bother about immediate side effects of the implant (i.e., side effects attributable to the implant procedure, occurring within the first few hours of administration), (7) bother about long-term side effects of the implant (i.e., side effects attributable to the sustained-release drug), (8) physical comfort

Table 3 Qualitative results of concept elicitation interviews: participants' most frequently reported considerations when rating satisfaction with implant treatment, and representative quotes

Concept	Representative quotes
Physical comfort during application of the implant	"It doesn't hurt"; "I didn't feel anything"
	"The administration itself is a little bit, it's a little uncomfortable"
	"And they numb your eye, but you can still kind of feel it, you're like okay that was uncomfortable, but then it was gone"
Feeling anxious about the procedure	"I was more nervous about that one [i.e., first implant administration]…because I wasn't sure exactly what was going to happen"
	"It was kind of scary because the idea of getting injections in my eye terrified me"
	"The second time I was still a little nervous but I knew what was going to happen…and the third time it was fine"
	"I have become less and less anxious about the procedure as time has gone on…I don't really have that much anxiety about it now"
Frequency of implant administration	"It's ten minutes and it's done. I don't have to worry about it for four months"
	"It would be nice if it lasted a little longer…I don't know if they don't last longer…four to six months would be nice"
Possible side effects	"I haven't had any complications"
	"My eyes were running. … I had puffy eyes. The next day I was pretty good…And then, this, the last two times I got red eyes"
Convenience and accessibility of the implant	"It's ten minutes and it's done. I don't have to worry about it for four months"
	"It was easy because it was quick…It was professional, it was quick. He knew what he was doing and I just listened and did what he said and it was quick…twenty minutes"
	"First, after they do the injections, then I have to wait an hour and then come back, and I usually sit in the lobby and I know my eyes are irritated and I just sit there"
Relationship with the clinician	"Kind, polite and efficient staff;" "very good about explaining everything"
	"She has got a soothing voice when she's telling me…it helps because I'm a little anxious"
Degree to which the implant experience fits with my lifestyle	"I just plan for it and I have my schedule at home and I more or less have an idea of what's going to happen"
	"There's no after effects in the injection, so there's really nothing that changes my routine"
	"I come here, I schedule my two hours or whatever, and then I go back to work"

Table 3 continued

Concept	Representative quotes
Physical comfort during preparation for the implant procedure	"There was no discomfort at all"
	"It's painful, not painful in the actual administration but in the preparation for getting ready…the actual process itself is not bad. It's just the prep, the prep is terrible"

during preparation for the implant procedure, (9) physical comfort during administration of the implant, (10) anxiety about receiving the implant, and (11) feeling scared or worried about potential risks or side effects of the implant. Two additional items, item 10a (did you feel anxious about the implant?) and item 11a (did you feel scared or worried about any potential risks or side effects of the implant?), were included in the instrument to explore alternative item wording and participant preference between items 10 and 10a, and 11 and 11a.

As the intention is to allow the ASTEQ Implant Experience instrument to be used at different timepoints during the course of a clinical study (i.e., after any implant administration), a non-specific recall period of "from the time you started this study until now" was chosen for the draft instrument. This provides flexibility as to when the instrument can be administered, and also enables participants to consider their cumulative experience with the implant.

Cognitive Debriefing Interview Findings

Cognitive debriefing interviews to assess the draft ASTEQ Implant Experience instrument were performed among a new set of 20 study participants who had previously been treated with sustained-release bimatoprost implants in the ARTEMIS trials. This sample ranged in age from 37 to 81 (mean 59.5) years, was predominantly White (65.0%) and non-Hispanic/Latino (65.0%) and comprised similar proportions of college graduates and non-graduates; most subjects had used topical IOP-lowering medication before enrolling in the study (75.0%) (Table 2).

Based on the cognitive debriefing interview findings, modifications were made to several items in the draft version of the ASTEQ Implant Experience instrument. Item 3 ("satisfaction with the convenience of receiving the implant") and item 5 ("satisfaction with the ease of following the implant treatment routine") were removed on grounds of conceptual redundancy with item 4 ("implant fit with routine or schedule"), which was felt to be more specific and understandable. Response options for item 6 ("bother about short-term side effects of the implant") and item 7 ("bother about long-term side effects of the implant") were modified to capture both the presence/absence of side effects and the degree of bother caused by side effects. The wording of item 8 ("physical comfort during preparation for the implant procedure"), item 9 ("physical comfort during administration of the implant"), item 10 ("anxiety about receiving the implant") and item 11 ("scared or worried about potential risks or side effects of the implant") was revised to improve clarity. Items 10a and 11a (alternative wordings for items 10 and 11) were removed, as items 10 and 11 were deemed to be conceptually less complex and more readily understood. Participants did not report that any additional concepts needed to be added to the draft ASTEQ instrument.

Revised PRO Instrument

Following implementation of recommendations arising from the cognitive debriefing interview, the revised ASTEQ instrument consisted of nine items assessing the following

Table 4 ASTEQ implant experience instrument: items and response options

ALLERGAN SATISFACTION WITH TREATMENT EXPERIENCE QUESTIONNAIRE (ASTEQ) GLAUCOMA OR OCULAR HYPERTENSION

IMPLANT EXPERIENCE MODULE

For use with sustained-release implants

VERSION 3.0

Instructions: This questionnaire includes questions about how satisfied you are with **receiving implants** to treat your glaucoma or ocular hypertension (OHT). **Do not** think about eye drops or other methods to treat your glaucoma or OHT. Please **only** think about your experience receiving implants to treat your glaucoma or OHT when answering these questions. Please **only** think about the eye that received the implant to treat your glaucoma or OHT when answering these questions.

Please select **one answer** that best describes your experience with implants **from the time you started this study until now**. There are no right or wrong answers.

1. How satisfied are you with the **overall experience** of receiving the implant to treat your glaucoma or OHT?

   ☐$_0$ Very satisfied

   ☐$_1$ Satisfied

   ☐$_2$ Neither satisfied nor dissatisfied

   ☐$_3$ Dissatisfied

   ☐$_4$ Very dissatisfied

2. Overall, how satisfied are you with **how often** you needed to receive the implant to treat your glaucoma or OHT?

   ☐$_{99}$ Not applicable – this is my first implant cycle

   ☐$_0$ Very satisfied

   ☐$_1$ Satisfied

   ☐$_2$ Neither satisfied nor dissatisfied

   ☐$_3$ Dissatisfied

   ☐$_4$ Very dissatisfied

3. Overall, how satisfied are you with how receiving the implant **fits with your routine or schedule?**

   ☐$_{99}$ Not applicable – this is my first implant cycle

   ☐$_0$ Very satisfied

   ☐$_1$ Satisfied

   ☐$_2$ Neither satisfied nor dissatisfied

   ☐$_3$ Dissatisfied

   ☐$_4$ Very dissatisfied

4. Overall, did you have any **immediate side effects** (lasting for up to 2 days) from receiving the implant to treat your glaucoma or OHT?

   ☐$_0$ No

   ☐$_1$ Yes, but the side effects did not bother me

   ☐$_2$ Yes, and the side effects were a little bit bothersome

   ☐$_3$ Yes, and the side effects were somewhat bothersome

   ☐$_4$ Yes, and the side effects were very bothersome

   ☐$_5$ Yes, and the side effects were extremely bothersome

Table 4 continued

5. Overall, did you have any **long-term side effects** (occurring after the first two days from treatment) from receiving the implant to treat your glaucoma or OHT?

   ☐$_0$ No

   ☐$_1$ Yes, but the side effects did not bother me

   ☐$_2$ Yes, and the side effects were a little bit bothersome

   ☐$_3$ Yes, and the side effects were somewhat bothersome

   ☐$_4$ Yes, and the side effects were very bothersome

   ☐$_5$ Yes, and the side effects were extremely bothersome

6. Overall, how **worried** did you feel about **receiving the implant**?

   ☐$_0$ Not at all worried

   ☐$_1$ A little worried

   ☐$_2$ Moderately worried

   ☐$_3$ Very worried

   ☐$_4$ Extremely worried

7. Overall, how **worried** did you feel about any **potential risks** or **side effects** of the implant?

   ☐$_0$ Not at all worried

   ☐$_1$ A little worried

   ☐$_2$ Moderately worried

   ☐$_3$ Very worried

   ☐$_4$ Extremely worried

8. Overall, how much **physical discomfort** did you experience during the **preparation for receiving the implant (for example, use of the tool to keep your eye open, lighting)?**

   ☐$_0$ No physical discomfort

   ☐$_1$ A little physical discomfort

   ☐$_2$ Some physical discomfort

   ☐$_3$ Quite a bit of physical discomfort

   ☐$_4$ A lot of physical discomfort

9. Overall, how much **physical discomfort** did experience when **receiving the implant itself (when the treatment was applied to the eye)?**

   ☐$_0$ No physical discomfort

   ☐$_1$ A little physical discomfort

   ☐$_2$ Some physical discomfort

   ☐$_3$ Quite a bit of physical discomfort

   ☐$_4$ A lot of physical discomfort

concepts: satisfaction with the overall experience of receiving the implant; satisfaction with how often the implant needs to be administered; satisfaction with how implant administration fits with one's routine or schedule; occurrence of any immediate side effects following implant administration and the degree of bother they cause; occurrence of any long-term side effects following implant administration and the degree of bother they cause; degree of worry about receiving the implant; degree of worry about any potential risks or side effects of the implant; level of physical discomfort experienced during patient preparation for implant administration; and level of physical discomfort experienced during actual implant administration (Table 4). The non-specific recall period of "from the time you started this study until now" chosen for the draft PRO instrument was retained for the revised version. Readability tests on the draft ASTEQ instrument identified several difficult words (predominantly words of three or more syllables). However, since participant feedback during cognitive interviews revealed no issues in interpretation of the instrument items, revisions to the wording were not recommended.

The conceptual framework was updated to reflect the contents of the revised ASTEQ instrument and modified to reflect the hypothesized relationships among the ASTEQ items. Proposed scoring of the ASTEQ instrument envisages its division into two domains: pretreatment concerns and treatment experience satisfaction, to be further evaluated in future psychometric validation (Fig. 2).

DISCUSSION

For patients prescribed topical IOP-lowering medication for ocular hypertension or open-angle glaucoma, difficulty with eyedrop administration and inability to maintain treatment compliance over the long term increase the risk of suboptimal IOP control and subsequent loss of visual function [30, 31]. Given that strategies to improve treatment compliance in these patients may help to preserve visual function [30, 32, 33], there is a need for treatment modalities that deliver IOP-lowering medication over an extended period without the need for daily eye drops. Sustained-release intracameral implants offer a drop-free, alternative drug-delivery option that circumvents the need for daily self-administration and potentially reduces the risk of periorbital and ocular surface adverse effects associated with topical administration [34–36]. Currently, the Durysta® 10 µg bimatoprost intracameral implant (AbbVie, North Chicago, IL, USA) is the only sustained-release glaucoma therapy approved by the FDA. Several other intracameral implants, including iDose® (Glaukos Inc, San Clemente, CA, USA), ENV515 Travoprost XR (Aerie Pharmaceuticals, Durham, NC, USA), and OTX-TIC (Ocular Therapeutix, Bedford, MA, USA) are in earlier stages of clinical development [37].

Given the likely future growth in the availability and use of sustained-release intraocular implants for treatment of ocular hypertension and glaucoma, there is a corresponding need for a validated PRO measure that can be applied in the clinical trial setting to quantify patient satisfaction with the experience of intraocular implant therapy. Accordingly, this study was undertaken with the purpose of developing, in line with FDA guidance recommendations [17, 18], a qualitative PRO instrument based on established qualitative research interviews conducted among patients who had received intraocular treatment with a sustained-release bimatoprost implant within the context of the phase 3 ARTEMIS studies [15, 16]. Concept elicitation interviews identified multiple factors that are important in shaping patients' impressions of satisfaction with the experience of intraocular implant therapy. These include more general glaucoma-related considerations stemming from the need for uninterrupted, lifelong treatment (e.g., frequency of treatment administration and ease of compliance) and treatment modality-related considerations (e.g., anxiety about receiving an intraocular injection, discomfort associated with the implant procedure, and worry about procedural mistakes and side effects with the implant). Cognitive debriefing interviews in turn provided valuable insight into ways of refining the

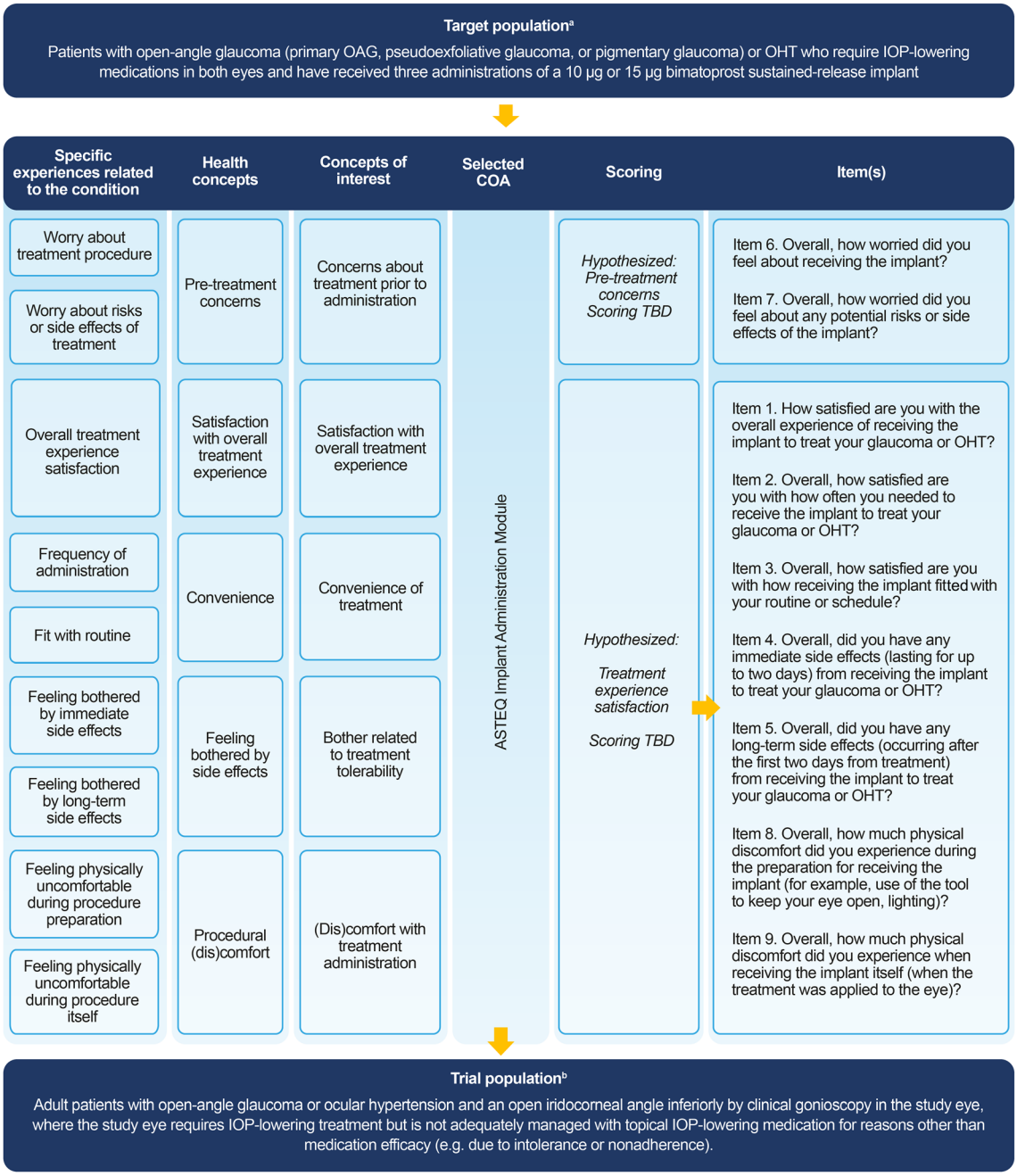

Fig. 2 Revised conceptual framework for assessing patient satisfaction with intraocular implant treatment experience in glaucoma. *COA* clinical outcome assessments, *IOP* intraocular pressure, *OAG* open-angle glaucoma, *OHT* ocular hypertension. [a]Target population comprises patients who completed the ARTEMIS 1 and ARTEMIS 2 studies of the bimatoprost sustained-release implant and were subsequently selected for participation in the concept elicitation and concept debriefing interviews. [b]Trial population comprises participants in an ongoing phase 3b study to evaluate the duration of effect of the bimatoprost sustained-release implant (NCT03850782), which incorporates a treatment satisfaction endpoint

suitability and interpretability of the draft PRO instrument (specifically, its instructions, the selection and wording of items for inclusion in the instrument, and the response options) to improve clarity for patients. As a consequence, the revised ASTEQ instrument was reduced to nine items capturing the following concepts: satisfaction with the overall implant experience, satisfaction with the frequency of implant administration, satisfaction with how implant administration fits with one's routine or schedule, occurrence and bother caused by immediate and long-term side effects of the implant, worry about the implant procedure, worry about possible risks and side effects of the implant, and physical discomfort arising during preparation for the implant and during administration of the implant.

Interviewees were required to have previously received three administrations of the bimatoprost implant at 4-month intervals during their participation in the ARTEMIS studies. It was hypothesized that as subjects gained more experience with the implant procedure, anxiety about the injection itself, and worry about possible procedural errors and side effects would decline. This was borne out by both sets of interviews, with the overall emotional impact of the implant experience (i.e., the combination of anxiety and worry) diminishing appreciably with each administration. This is likely to be an important consideration when administering the ASTEQ Implant Experience instrument in the clinical trial setting: it is anticipated that patients' reported satisfaction with a given treatment will improve over the course of multiple implant administrations as their initial feelings of anxiety and worry are gradually allayed. The choice of a non-specific recall period of "from the time you started this study until now" for the ASTEQ instrument may, however, require refinement, as this is likely to blur the ability to distinguish between issues related to implant administration and ongoing implant residence.

A potential limitation of this study is that the systematic literature review undertaken to identify available PRO instruments for assessing treatment satisfaction in glaucoma was performed several years ago (2015). However, a search of the more recent literature (2016–July 2023), employing various databases (MEDLINE via PubMed, PROQOLID, and PROLabels) and our original search terms, likewise indicates that current PRO measures in glaucoma have limited applicability in assessing patients' experience with intraocular implants. Therefore, we can conclude that the rationale for introducing the ASTEQ instrument into clinical practice is still valid.

CONCLUSION

The ASTEQ Implant Experience instrument has been developed using rigorous qualitative research analysis methods to be consistent with current FDA recommendations for PRO measures for use in drug registration trials [17]. The instrument assesses, in a clear and understandable manner, those concepts that are important and relevant to patients undergoing intraocular implant therapy for ocular hypertension or open-angle glaucoma. Work remains to evaluate the psychometric performance of the instrument among this patient population and to determine its ability to demonstrate quantitative changes in patient satisfaction with the implant treatment experience in the clinical trial setting.

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Data Availability. AbbVie is committed to responsible data sharing regarding the studies we sponsor. This includes access to analysis data sets, as well as other information (e.g., protocols, study reports, or analysis plans), as long as the studies are not part of an ongoing or planned regulatory submission. These study data can be requested by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal, statistical analysis plan (SAP), and execution of a data sharing agreement (DSA). Data requests can be submitted at any time after approval in the USA and Europe (if applicable) and after acceptance of this manuscript for publication. The data will be accessible for 12 months, with possible extensions considered. For more information on the process, or to submit a request, visit the following link: https://www.abbvieclinicaltrials.com/hcp/data-sharing/.

Declarations

Conflict of Interest. Joice T. Huang and Margot L. Goodkin are employees of AbbVie Inc. Martha Gauthier is an employee of Lumanity, which has a research consultancy agreement with AbbVie. Richard Evans declares that he has no competing interests.

Ethical Approval. All subjects provided their written informed consent to participate in the study, and written authorization to access personal health information in accordance with the US Health Insurance Portability and Accountability Act (HIPAA).

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