Understanding the Patient Experience with Carcinoid Syndrome: Exit Interviews from a Randomized, Placebo-controlled Study of Telotristat Ethyl

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ABSTRACT

Purpose: Telotristat ethyl, an oral tryptophan hydroxylase inhibitor, is intended to treat carcinoid syndrome by reducing serotonin production. Telotristat ethyl was evaluated in TELESTAR, a Phase III study for patients who had carcinoid syndrome with at least 4 bowel movements (BMs) per day and who were receiving somatostatin analogue therapy. This interview substudy was conducted to provide insight into the patient experience in TELESTAR and to help understand whether reductions in BM frequency (the primary end point) and other symptoms were clinically meaningful.

Methods: Participating sites were asked to invite (before randomization) all eligible patients to telephone interviews scheduled at the end of the double-blind treatment period. Patients and interviewers were blinded to treatment.

Findings: All 35 interviewed participants reported diarrhea and/or excessive BMs at baseline. Patients reported that these symptoms negatively affected emotional, social, physical, and occupational well-being. Prespecified criteria for treatment response (achieving ≥30% reduction in BM frequency for at least 50% of the days) were met by 8 of 26 patients taking telotristat ethyl and 1 of 9 patients taking placebo. All 8 patients taking telotristat ethyl described clinically meaningful reductions in BM frequency and were very satisfied with the ability of the study drug to control their carcinoid

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syndrome symptoms. Overall, reports of being very satisfied were observed in 12 patients taking telotristat ethyl and 0 taking placebo.

Implications: Patient interviews revealed that TELESTAR patients, at baseline, were significantly affected by their high BM frequency. Patient reports of their clinical trial experience supported the significance of the primary end point and clinical responder analysis in TELESTAR, helping identify and understand clinically meaningful change produced by telotristat ethyl. (*Clin Ther*. 2017;39:2158–2168) © 2017 The Authors. Published by Elsevier HS Journals, Inc.

Key words: bowel movement, carcinoid syndrome, diarrhea, exit interviews, patient interviews, telotristat ethyl.

INTRODUCTION

Well-differentiated neuroendocrine tumor (NET), formerly known as carcinoid tumor, is a relatively rare tumor type that arises from cells of the diffuse neuroendocrine cell system.[1,2] Carcinoid syndrome occurs when well-differentiated NET secretes large amounts of serotonin and other vasoactive products into the systemic circulation. Classically, symptoms associated with carcinoid syndrome include cutaneous flushing, diarrhea, wheezing, abdominal pain, and valvular heart disease.[3] The prevalence of well-differentiated NET is approximately 50,000 cases in any 1 year in the United States, as reported by Vinik et al.[4] A detailed analysis based on Surveillance, Epidemiology, and End Results data[5] estimates the 2004 prevalence of NET to be 103,312 cases.[2] Well-differentiated NETs represent approximately half of all NETs.[6] However, not all well-differentiated NETs will result in carcinoid syndrome. It has been estimated that 10% of all patients with well-differentiated NETs will develop carcinoid syndrome.[7] Approximately 75% of patients with carcinoid syndrome will experience diarrhea.[8,9]

The most common symptoms of carcinoid syndrome include diarrhea, paroxysmal facial flushing, difficulty breathing, rapid heartbeat, and right-sided heart disease or failure.[10–13] These symptoms are the result of biochemical secretions (most prominently serotonin for diarrhea) from carcinoid tumors into the bloodstream.[10] Patients with carcinoid syndrome have various combinations of these symptoms. Several studies[14,15] have found that patients experiencing 2 of the most common symptoms of carcinoid syndrome, flushing and diarrhea, have significantly impaired quality of life. Among patients with carcinoid syndrome who report increased frequency of bowel movements (BMs), health-related quality-of-life impairments are worst in those reporting ≥4 BMs per day.[14]

In addition to treatment of the underlying tumor disease, patients with carcinoid syndrome typically receive medications to control specific symptoms, including injections of somatostatin analogues, such as octreotide or lanreotide, to help control diarrhea along with conventional antidiarrheal therapy.[10,16] Telotristat ethyl, an oral tryptophan hydroxylase inhibitor, may improve carcinoid syndrome symptoms by reducing serotonin production by NET cells. Telotristat ethyl was evaluated in TELESTAR, a phase III placebo-controlled study for patients with carcinoid syndrome diarrhea, who were receiving somatostatin analogue therapy and who had uncontrolled BMs (mean, ≥4 per day). One hundred thirty-five participants were randomized 1:1:1 to receive placebo TID or telotristat ethyl (250 or 500 mg) TID. The primary end point of the TELESTAR study was the change from baseline in the number of daily BMs averaged during a 12-week, double-blind treatment period. TELESTAR methods and the pivotal study results have been described previously.[17]

Briefly, estimated differences from baseline in BM frequency versus placebo averaged during 12 weeks were –0.81 and –0.69 BMs per day for telotristat ethyl 250 mg ($P < 0.001$) and 500 mg ($P < 0.001$), respectively. At week 12, mean BM frequency reductions for placebo, telotristat ethyl 250 mg, and telotristat ethyl 500 mg were –0.9, –1.7, and –2.1 BMs per day, respectively. Durable responses, predefined as BM frequency reductions of ≥30% from baseline for ≥50% of the double-blind treatment period, occurred in 20%, 44%, and 42% of patients given placebo, telotristat ethyl 250 mg, and telotristat ethyl 500 mg, respectively. The overall incidences of adverse events and treatment discontinuation were similar between the groups.

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30), which was assessed among all randomized patients in the study, has the value of being assessed systematically in all patients and being supported by prior scientific literature, whereas the

exit interviews provide a more individualized and qualitative understanding that directly connects patient symptoms and experiences. Qualitative interviews conducted with patients exiting a phase II clinical trial of telotristat ethyl signaled the importance and effect of BM frequency[18]; however, a more robust understanding of the patient experience with carcinoid syndrome (both before and during treatment) was desired for TELESTAR. Therefore, the aim of the present study was to explore patients' experiences with carcinoid syndrome and the extent to which, if at all, treatment affected their experiences by conducting prospective, qualitative exit interviews with volunteers from TELESTAR. Specific objectives of the interview study included (1) gaining a comprehensive understanding of patients' experiences with carcinoid syndrome before the start of the TELESTAR study; (2) identifying, from the patient perspective, which symptoms were most important to treat and most bothersome; (3) assessing patients' perspectives on the treatment benefit of blinded study drug; (4) gathering further insight into the relevance and clinical meaningfulness of specific symptom improvements (such as reduction in BM frequency); and (5) assessing patient satisfaction with telotristat ethyl. The conduct of this qualitative exit interview study was identified as the optimal method to assess the full effect of symptoms, the relative importance of symptoms, and the meaningfulness of symptom improvement directly from patients.

METHODS

Clinical sites in 5 countries (Australia, Canada, England, Germany, and the United States) invited participants in the TELESTAR clinical study to take part in an exit interview after their end-of-treatment visit at week 12. These 5 countries (of 12) were selected to maximize enrollment while limiting the number of languages required. All interview procedures were prespecified in the TELESTAR protocol and were approved by ethics committees; all participants in the exit interview study provided written informed consent. Interviews were conducted by telephone in English or German approximately 2 weeks after a patient's end-of-treatment visit by senior researchers in the Patient-Reported Outcomes Division at RTI Health Solutions (Research Triangle Park, North Carolina), a pharmaceutical/biotech consulting research organization. Patients, clinical sites, and interviewers were blinded to treatment group assignment. All interviews were audio recorded and transcribed.

Each interview was conducted using a semistructured interview guide and was divided into 2 phases. Phase I of the interview focused on the patient's carcinoid syndrome symptom experiences before the study. Patients were asked open-ended questions to identify (and define in their own words) a comprehensive list of their carcinoid syndrome symptoms. Once an exhaustive list of symptoms associated with carcinoid syndrome was elicited, ranking methods were used to narrow the full list of carcinoid syndrome symptoms to include only those of greatest importance to each patient. Specifically, patients were asked to report the 3 symptoms they most wanted to see improve with treatment and then to rank these symptoms in order of importance. Patients were then queried about the daily effect of their carcinoid syndrome symptoms (eg, how, if at all, their carcinoid syndrome affected their lives and if certain symptoms were more impactful than others). Phase II of each interview focused on carcinoid syndrome symptom experiences or changes during the clinical trial and the importance of these changes. Interview participants were asked to report all improvements (of any magnitude) noticed during the clinical trial and to discuss the relative importance of these improvements. To further quantify the degree of change experienced (if any) during the clinical trial, 3 questions were asked during the interviews (Table I). To our knowledge, these questions had not been used previously in carcinoid syndrome research. They were developed with standard Likert scales to address study objectives.

Interview data were summarized with standard qualitative analysis methods using field notes and interview transcripts. RTI Health Solutions developed a codebook to facilitate the consistent categorization and organization of carcinoid syndrome symptoms and effects. Analyses of the quantitative items collected during the exit interviews (questions 1-3) and selected clinical data (specifically, change in BM frequency and durable response defined as ≥30% reduction in BM frequency for ≥50% of the treatment period) were conducted by the TELESTAR study's sponsor and are included in this article.

Table I. Interview questions.

Question 1. Since you started the study medication, would you say that the number of your bowel movements *now* is...

1. A great deal better
2. Much better
3. A little better
4. The same
5. A little worse
6. Much worse
7. A great deal worse

Question 2. Since you started the study medication, would you say your stool consistency/form *now* is...

1. A great deal better
2. Much better
3. A little better
4. The same
5. A little worse
6. Much worse
7. A great deal worse

Question 3. Overall, how satisfied are you with how the study medication relieved your carcinoid syndrome symptoms?

1. Very satisfied
2. Somewhat satisfied
3. Neither satisfied nor dissatisfied
4. Somewhat dissatisfied
5. Very dissatisfied

RESULTS

Participant Demographic Characteristics

A total of 35 patients, of the 135 randomized cohort patients recruited across 16 clinical sites and 5 countries, completed the exit interview study. Table II presents the specific demographic characteristics of patients participating in the interview substudy and the overall TELESTAR study. All interviews were conducted between July 2, 2013, and June 15, 2015.

Carcinoid Syndrome Symptom Experiences Before Study

Interview participants (n = 35) reported experiencing many symptoms related to carcinoid syndrome before starting the clinical trial. BM-related symptoms were reported most frequently (ie, too frequent BMs, diarrhea, loose and watery stools, and urgent BMs). Table III provides a summary of the carcinoid syndrome–related symptoms that ≥20% of participants reported experiencing at baseline.

Too-frequent BMs were the most frequently reported carcinoid syndrome symptom (34 [97%]). Selected quotations describing this concept in participants' own words are as follows: "I was up over 10 times a day, which wasn't really acceptable."; "I did have days where, you know, 2 minutes after I had left the bathroom, I'd have to be going back. So those, probably 15, 20 times a day."; and "I'd say anywhere between 5 to 12 as a rule, occasionally more than that. Occasionally it would get up to maybe 17, 18. But definitely most days [average] would be 12, 11 to 12."

Participants commonly described diarrhea as a multifaceted concept that included >1 BM-related symptom (most common: loose, watery stools [n = 28]; too frequent BMs [n = 22]; and urgent BMs [n = 16]). Selected quotations describing these concepts in participants' own words are as follows: "Uncontrollable diarrhea … It means 5 plus trips to the bathroom … plus the uncontrollable piece … where you have to go and there's no stopping it. You can't get to a bathroom fast enough."; "When all I had to do was try to move or walk, and I had to go running to the toilet… But by diarrhea, I mean I'm going to the toilet, you know, 5, 10, 15 times a day."; and "I mean, I practically had diarrhea around the clock… It's always runny… the problem with it is that it's difficult to control because my entire life or day is scheduled around where the nearest toilet is."

Most Important to Treat and Most Bothersome Carcinoid Syndrome Symptoms

Interview participants' reports of the 3 most important symptoms to treat and the 3 most bothersome symptoms were highly consistent. Diarrhea (n = 17), BM frequency (n = 9), and urgency (n = 5) were most frequently identified as the most important carcinoid syndrome symptom to treat (ie, most frequently reported as number 1 of the top 3 symptoms to treat).

Table II. Participant demographic characteristics.

Characteristic	Interview Substudy (n = 35)	Overall TELESTAR Study (n = 135)
Age, mean, y	62	64
Female, %	51	48
White, %	97	90
Baseline body mass index, mean, kg/m^2	26	25
Baseline BM frequency, BMs/d	5.76	5.70
Mean BM frequency reduction during 12 weeks, BMs/d	−1.11	−1.17

BM = bowel movement.

These 3 symptoms also were ranked as the most bothersome symptoms by all but 2 interview participants. For 29 of the 35 interview participants (83%), BM frequency was reported as being more important to treat than stool form or consistency. Twelve of 19 respondents (63%) reported that BM frequency was the most important aspect of their diarrhea to treat, followed by urgency in 8 of 19 (42%). None of these participants reported stool form/consistency as the most important aspect of their diarrhea to improve.

Table III. Carcinoid syndrome–related symptoms that ≥20% of interview participants reported experiencing at baseline.

Symptom	Total No. (%) (n – 35)
BM-related symptoms	
Too frequent BMs	34 (97)
Diarrhea	33 (94)
Loose, unformed, or watery stools	33 (94)
Urgent BMs	30 (86)
Accidents	16 (46)
Abdominal symptoms	
Abdominal pain and/or discomfort	22 (63)
Nausea	14 (40)
Cramping	7 (20)
Other symptoms or effects	
Flushing	30 (81)
Low energy	22 (63)
Rapid heart rate, shortness of breath, or wheezing	7 (20)

BM = bowel movement.

Effect of Carcinoid Syndrome Symptoms

Negative effects of carcinoid syndrome symptoms on social and physical activities and hobbies were reported most frequently, closely followed by emotional and energy areas (Table IV). Interview participants indicated that certain carcinoid syndrome symptoms had greater effect on their lives than others, with too frequent BMs (n = 24) followed by urgent BMs as the most commonly reported impactful symptoms (n = 14). Selected quotations describing these concepts in participants' own words elucidate the effect on patients: "Because [frequent BMs are] the most disruptive. You can't do anything. You can't walk around the block. You can't take your kid to the park. You're homebound."; Well, because diarrhea, it's just so socially absurd. I mean, I couldn't do anything. I'd be afraid to go out of the house."; and When my son got married … he asked me to be his best man. And I had to turn him down. I told him that there's a good possibility I might have to leave the altar if I had to go to the bathroom. I also had to give up my career, because … you cannot go to the bathroom when you teach school."

Treatment Experiences and Changes

Of the 35 interview participants (placebo:250 mg:500 mg = 9:10:16), 34 provided information on treatment experience. Among them, 24 participants (placebo:250 mg:500 mg = 4:7:13) reported improvements in their carcinoid syndrome symptoms.

Table IV. Effect of carcinoid syndrome symptoms reported by ≥20% of interview participants.

Adverse Effect	Frequency of Reports, No. (%) (n = 35)
Social and/or physical activities and hobbies	28 (80)
Emotional	24 (69)
Decreased energy	21 (60)
Occupational (work in and outside the home)	15 (43)
Travel	15 (43)
Sleep	15 (43)

Among these, 21 participants reported their improvements as meaningful or important.

Too frequent BMs was the symptom for which interview participants most frequently reported improvements (n = 21) (placebo:250 mg:500 mg = 4:7:10), and 20 of 21 participants (95%) who reported reductions in BM frequency noted that the reduction experienced was meaningful to them (placebo:250 mg:500 mg = 3:7:10). When probed as to why this improvement was meaningful, participants consistently reported that their ability to enjoy life, leave the house, and participate in social and other activities had been improved by their reduction in BM frequency. Nearly two-thirds of the patients who reported an improvement in their BM frequency indicated that their BMs were "a great deal better" or "much better." Selected quotations describing these concepts, in participants' own words, are as follows: "I definitely feel like I'm not a prisoner in my house, staying 10 feet to the nearest bathroom. I can go out to activities." And "But the biggest change is not having to run to the toilet constantly … You can't live going 20 times a day. I was able to go out more often."

To further understand the significance of incremental changes in BM frequency, participants were also asked to report the smallest reduction in BM frequency that they would consider meaningful. Patients with more frequent BMs at baseline generally reported that a greater reduction in BM frequency would be needed to have a meaningful change compared with those with less frequent BMs at baseline (or to move toward normalcy). Because >30% reduction in BM frequency had been the prespecified criterion used for the responder analysis in the double-blind randomized trial, we used the same threshold here to analyze study participant responses in the exit interviews. Most participants who provided a response (n = 17/28 [60.7%]) responded with a threshold of ≤30% reduction.

Analyses of Quantitative Interview Items

Among the 33 interview participants (placebo: 250 mg:500 mg = 9:9:15) answering the interview question about treatment satisfaction (question 3) (Table I), 58% across all 3 treatment arms reported being somewhat or very satisfied with the treatment they received during the TELESTAR study (placebo; 250 mg:500 mg = 3:6:10). Patients with greater satisfaction reported greater reduction in BM frequency (Figure 1). The association between responses to questions was examined using the Pearson correlation coefficient. A positive correlation ($R = 0.66$, $P < 0.001$) was seen between reported change in the BM frequency question (question 1) (Table I) and treatment satisfaction (question 3) (Table I). In addition, a significant correlation ($R = 0.54$, $P < 0.001$) was seen between reported change in the stool form question (question 2) (Table I) and treatment satisfaction (question 3) (Table I).

All participants who reported satisfaction reported a reduction in BM frequency, except for one individual, a participant taking placebo who was only somewhat satisfied and described minimal changes until open-label treatment began. None of the 9 patients taking placebo reported being very satisfied (question 3), whereas 12 of the 24 patients (50%) taking telotristat ethyl reported being very satisfied with treatment (Figure 2).

Durable response was a predefined definition of clinically meaningful change in the TELESTAR study (at least 30% reduction in BM frequency observed on at least 50% of days in the study). Among the 9 interview participants with durable responses, one was taking placebo and was neither satisfied nor dissatisfied. The other 8 were taking telotristat ethyl, and all 8 participants (100%) reported being very satisfied with the ability of study drug to control their carcinoid syndrome symptoms. All 8 reported meaningful improvement in BM frequency. Only 1 of 8 experienced a BM frequency reduction smaller than his/her reported threshold for clinically meaningful change: the patient experienced a 43% reduction

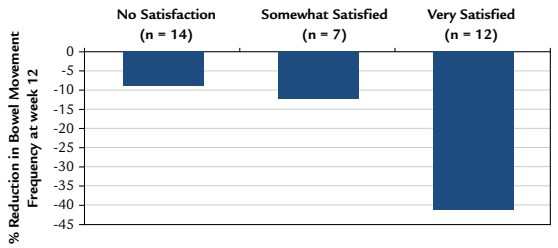

Figure 1. Relationship between treatment satisfaction and percentage reduction in bowel movement (BM) frequency at week 12. Treatment satisfaction is reported in the context of question 3 (*Table I*). BMs were reported daily on electronic diaries during the TELESTAR study. Sample size was 33 from pooled treatment arms (placebo: telotristat = 9:24). Patients who answered 3, 4, or 5 to the treatment satisfaction question were grouped into the category no satisfaction.

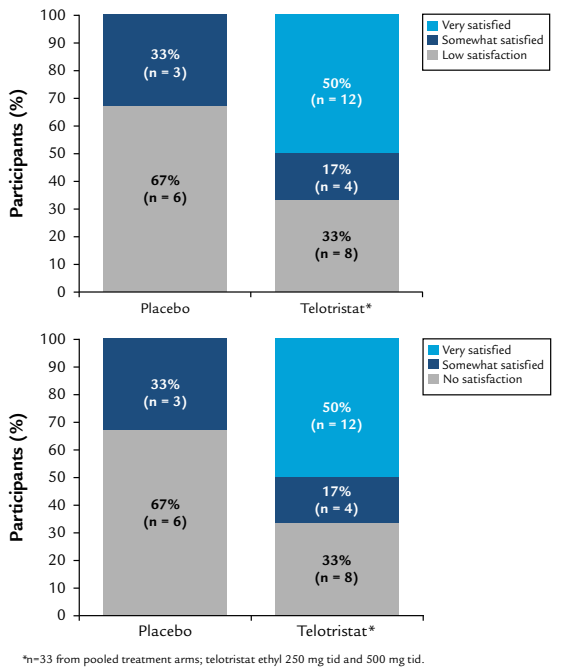

Figure 2. Reports of treatment satisfaction by treatment group. For the telotristat group, n = 33 from pooled treatment arms (telotristat ethyl 250 mg TID and 500 mg TID).

averaged during 12 weeks and described his own reduction as meaningful and was very satisfied, but the responses indicated a 55% reduction as a threshold for clinically meaningful change.

Four patients reported being very satisfied without achieving criteria for durable response. One of them had no reduction in BM frequency at week 12, whereas the others were in the range of 10% to 20% reductions. They all described changes in BM frequency as being small while pointing to related benefits in gastrointestinal symptoms. All of them spoke about reductions in urgency and improvements in stool consistency. Two emphasized strongly an increase in energy as an important benefit, and one of them was also encouraged by weight gain as a sign of improved gastrointestinal function.

Among the interview participants, 8 reported adverse events (placebo:250 mg:500 mg = 2:2:4). These were communicated to Lexicon Pharmaceuticals, who ensured that they were all captured in the safety database. Adverse events on placebo included a report of increased BM frequency and worsening stool form and a report of flushing, fatigue, and fogginess. Both adverse events in the 250-mg group were of abdominal pain (one accompanied by facial flushing). Adverse event reports in the 500-mg group were abdominal pain, constipation with nausea, flushing, and dizziness with lightheadedness and weight loss (1 patient each).

DISCUSSION

Patients with carcinoid syndrome have impaired of quality of life.[14] The objective of this exit interview study was to better understand the experiences of patients with carcinoid syndrome (eg, symptoms experienced and effects of those symptoms) and to obtain insight into the relevance and clinical meaningfulness of specific symptom improvements and their associated impact. Elicitation of this information directly from patients participating in a clinical trial of telotristat ethyl for the treatment of carcinoid syndrome yielded a number of important findings.

Participants' descriptions of the most salient symptoms of carcinoid syndrome were highly consistent and generally focused on BM-related symptoms, specifically BM frequency. All interview participants reported experiencing at least too frequent BMs or

diarrhea at baseline, and only 1 participant did not initially report too frequent BMs as a symptom. Patients described diarrhea as a multifaceted symptom driven not only by stool form and consistency but also by frequency and urgency. Participants consistently reported that BM frequency was the most important and most bothersome aspect of their diarrhea to treat, and most participants (83%) reported that an improvement in BM frequency was more important than an improvement in stool form or consistency.

Participants also described the effect their carcinoid syndrome symptoms had on their lives as significant. This effect included emotional effects (anxiety about leaving their homes and potentially not finding a bathroom), the inability to engage in social activities (social activities and hobbies) and physical activities (such as exercise), and difficulty retaining employment (occupational and financial). When asked what symptoms had the greatest effect, participants reported too frequent BMs more often than any other symptom.

Most interview participants across treatment groups (62%) reported a reduction in their BM frequency by the end of the clinical trial, and all but 1 of these participants noted that this improvement was meaningful. Participants who experienced a meaningful reduction in BM frequency reported improvements in emotional well-being and social and physical functioning. Furthermore, 81% of participants who reported an improvement in BM frequency reported being either somewhat satisfied or very satisfied with the study medication. The highest level of treatment satisfaction was reported only with telotristat ethyl not placebo.

Taken together, these findings indicate the substantial burden patients with carcinoid syndrome experience and that too frequent BMs play an integral role in this burden. The interview data clearly support the importance of the TELESTAR study's primary end point: change in BM frequency. The interview results also support the relevance of the prespecified responder analysis (≥30% reduction in BM frequency) because all patients taking telotristat ethyl who met responder criteria were very satisfied with treatment. These results assist in the interpretation of the clinical trial data and further support the clinical meaningfulness of the symptom changes reported in the TELESTAR study.

This understanding is important because numeric changes in BM frequency can be difficult to interpret. Some experts have been cautious in describing the meaning and magnitude of clinical trial results.[19] This interview study may provide a useful guide. It suggests that BM frequency reductions in TELESTAR were sufficient to have a substantial effect on the lives of patients with carcinoid syndrome.

Poor stool consistency was a problem for many patients, but improving stool consistency was not as important as reducing BM frequency. Interview transcripts did not directly link stool consistency to physical or social function. When some patients communicated a desire for better stool consistency, they described it as a sign of better gastrointestinal function. In contrast, the large number of BMs was directly limiting the lives of patients.

During TELESTAR, the QLQ-C30 and European Organisation for Research and Treatment of Cancer Gastrointestinal Neuroendocrine Tumours questionnaires[20] were applied to all patients. These questionnaires provided a systematic assessment supported by prior scientific literature, complementing the exit interview data that connected patient symptoms and experiences. In the QLQ-C30, diarrhea subscale arithmetic mean scores averaged during the 12-week study period improved by 19.2 and 21.6 points (on a rating scale of 0 to 100) in the telotristat ethyl 250 mg TID and 500 mg TID groups, respectively, and by only 8.5 in the placebo group ($P = 0.039$ for telotristat ethyl 250 mg and $P = 0.051$ for telotristat ethyl 500 mg compared with placebo). Changes greater than 10 are considered clinically meaningful.[21] These results are consistent with those of the exit interview study.

The design of this qualitative exit interview study has several advantages and limitations. When conducted with scientific rigor and expertise, qualitative research of this type has the potential to further explain clinical trial findings, ensure interventions meet the needs of health care professionals and patients, and ensure that the right instruments are used to measure the outcomes of interest.[22] In this case, the feedback of interview participants characterizes the effect of the symptoms of carcinoid syndrome on patients' lives and emphasizes the importance of a reduction in BM frequency, thus supporting the primary end point and responder analysis of the TELESTAR study.

The decision to perform the interviews as a substudy related to logistics and sample size considerations. Logistically, there was concern that an effort to include many more patients would require more

personnel and translations, potentially introducing inconsistencies in the data. A prior study in the area of rheumatoid arthritis with disease flares had suggested that 20 interviews were sufficient to provide reliable and valid interpretations of subjective well-being.[23] Therefore, we believed that the sample of 35 patients would likely provide a reasonable assessment of how carcinoid syndrome affected patients' lives.

There was no formal validation exercise conducted as part of this study. Such an exercise would be standard in the development of an itemized questionnaire intended for systematic, quantitative assessments and repeated use in different settings. Instead, this study was intended to broadly describe and identify patient perspectives in TELESTAR. The close relationships between observed BM frequency change in TELESTAR and interview responses suggest that relevant perspectives were identified.

That said, caution should be used in interpreting findings from this study. Although all participants easily described their experiences with carcinoid syndrome before and during the TELESTAR trial, a limitation of this study is the recall bias involved in thinking back over a 12-week treatment period. In addition, the sample size was limited, so the results should be treated as a description of the trial experience rather than as an exercise in testing specific hypotheses for statistical significance. A common concern is that patients who choose to participate in interviews are those who experience a more favorable outcome, but participants in this study were invited and scheduled to participate in interviews before randomization. Their reductions in BM frequency were not any greater than that of the overall TELESTAR study.

It is also important to compare the characteristics of this subset of patients to those overall in the TELESTAR study. The demographic characteristics and even BM frequency reductions seen in the interview data were similar to those of the TELESTAR study overall, yet it would be ideal in future exercises to include all clinical study patients if feasible.

CONCLUSION

The results of this exit interview indicate that frequent and urgent BMs were the most important symptoms to treat. Participants reported that improvements in these symptoms allowed them to better enjoy life, leave the house, and participate in social and other activities. These patient perspectives support the significance of the primary end point and clinical responder analysis in the TELESTAR study, helping identify and understand clinically meaningful changes produced by telotristat ethyl.

CONFLICTS OF INTEREST

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L. Law was an employee of Lexicon Pharmaceuticals Inc during the study design but not during the conduct of the study. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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Lowell Anthony contributed to patient recruitment, interpretation of results, and writing of the manuscript. Claire Ervin contributed to design of the study, conduct of the interviews, the data analysis plan, data analysis, interpretation of results, and writing of the manuscript.

Pablo Lapuerta contributed to design of the study, the data analysis plan, data analysis, interpretation,

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