

Assessing Treatment Benefit of Telotristat Etiprate in Patients With Carcinoid Syndrome: Patient Exit Interviews

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Background

- Carcinoid syndrome (CS) often causes diarrhea, flushing, abdominal pain, fatigue, and other symptoms, impairing quality of life.^{1,2}
- Telotristat etiprate (TE), an oral tryptophan hydroxylase inhibitor, is intended to treat CS by reducing serotonin production in metastatic neuroendocrine tumor cells.
- Telotristat etiprate was evaluated in TELESTAR, a phase 3 placebo-controlled study for patients with inadequately controlled CS, on somatostatin analog therapy, who experienced at least 4 bowel movements (BMs) per day. Patients were randomized 1:1:1 to receive placebo tid or TE (250 mg and 500 mg) tid.
- TELESTAR'S primary endpoint was the change from baseline in the number of daily BMs averaged over a 12-week double-blind treatment period. Patients experienced significant reductions in BM frequency for both TE dosages versus placebo.
- Patients were interviewed as they exited the randomized treatment portion of TELESTAR.

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

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

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

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

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

- Interview data were summarized with standard qualitative analysis methods using field notes and interview transcripts.
- The relationships between responses to Questions 1-3 and changes in BM frequency observed in TELESTAR were examined.

Results

- A total of 35 patients recruited across 16 clinical sites and 5 countries completed the exit interview study. All interviews were conducted between 02 July 2013 and 15 June 2015.

CS Symptom Experiences Before the Study

- Participants reported experiencing a large number of CS symptoms before starting the clinical trial (Table 1).
- BM-related symptoms were reported most frequently (ie, too frequent BMs, diarrhea, loose and watery stools, and urgent BMs).

TABLE 1: CS Symptoms Experienced Before the Clinical Trial (N = 35)

Symptom	Total Count N (%)
BM-related symptoms	
Too frequent BMs	34 (97)
Diarrhea	33 (94)
Loose/unformed/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 impacts	
Flushing	30 (81)
Energy	22 (63)

Note: Table includes CS symptoms reported by at least 20% of participants. N = 35 from pooled treatment arms.

- Too frequent BMs was the most frequently reported CS symptom. Comments included:
 - "...I was up over 10 [BMs] a day, which wasn't really acceptable..."
 - "...I felt like I was living in my bathroom all the time."
- Participants commonly described diarrhea as a multifaceted concept that included more than 1 BM-related symptom (most commonly, loose, watery stools [n = 28]; too frequent BMs [n = 22]; and urgent BMs [n = 16]).
 - "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... At first I had a lot of just really, really watery stools...But by diarrhea, I mean I'm going to the toilet, you know, 5, 10, 15 times a day."

Most Important to Treat/Most Bothersome CS Symptoms

- 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 identified as the most bothersome and most important symptoms to treat (Table 2).
- In 83% of interview participants (29 of 35), BM frequency was reported as being more important to treat than stool form/consistency.
- The majority of respondents reported that BM frequency was the single most important aspect of their diarrhea to treat (60%), followed by urgency (40%). None of these participants reported stool consistency as the single most important aspect of their diarrhea to improve.

TABLE 2: The Most Important CS Symptoms to Treat (N = 35)

Symptom	Among the 3 Most Important Symptoms n (%)	Single Most Important Symptom n (%)
Diarrhea	19 (54)	17 (49)
Too frequent BMs	17 (49)	9 (26)
Flushing	16 (46)	2 (6)
Urgent BMs	12 (34)	5 (14)
Stool form/consistency	7 (20)	0

Note: Table includes CS symptoms reported by at least 20% of participants as among the 3 most important CS symptoms to treat. N = 35 from pooled treatment arms.

Impact of CS Symptoms

- Negative impacts of CS symptoms on social/physical activities/hobbies were reported most frequently, closely followed by emotional and energy areas (Table 3).

TABLE 3. CS Symptoms Areas of Impact (N = 35)

Symptom	Frequency of Reports n (%)
Social and/or physical activities/hobbies	28 (80)
Emotional	24 (69)
Energy	21 (60)
Occupational (work in and outside the home)	15 (43)
Travel	15 (43)
Sleep	15 (43)

Note: The table includes the CS symptom impacts reported by at least 20% of participants. The sum exceeds 100%, as participants often reported multiple impact areas. N = 35 from pooled treatment arms.

- Too frequent BMs was the most frequently reported, most impactful CS symptom (Table 4).
- Quotes describing the most impactful CS symptoms included:
 - "Because [frequent BMs is] 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."
 - "I also had to give up my career, because... I am an elementary school teacher and you cannot go to the bathroom when you teach school."

TABLE 4: Most Impactful CS Symptoms (N = 35)

Symptom	Frequency of Reports n (%)
Too frequent BMs	24 (69)
Urgency	14 (40)
Diarrhea	8 (23)
Energy	5 (14)

Note: Table includes the most impactful CS symptoms reported by at least 2 participants. The sum exceeds 100% as participants could report more than 1 most impactful symptom(s). N = 35 from pooled treatment arms.

Clinical Trial Experiences/Changes

- Too frequent BMs was the most frequently reported symptom improved (Table 5), and 95% of participants who reported reductions in BM frequency (20 of 21) noted that the reduction experienced was meaningful to them, allowing them to better enjoy life, leave the house, and participate in social and other activities.
- Related quotes included the following:
 - "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..."
 - "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..."
- Most participants reported that a BM frequency reduction of at least 30% would be considered meaningful.

TABLE 5: Frequency of Self-reported Symptom Improvement During TELESTAR (N = 24)

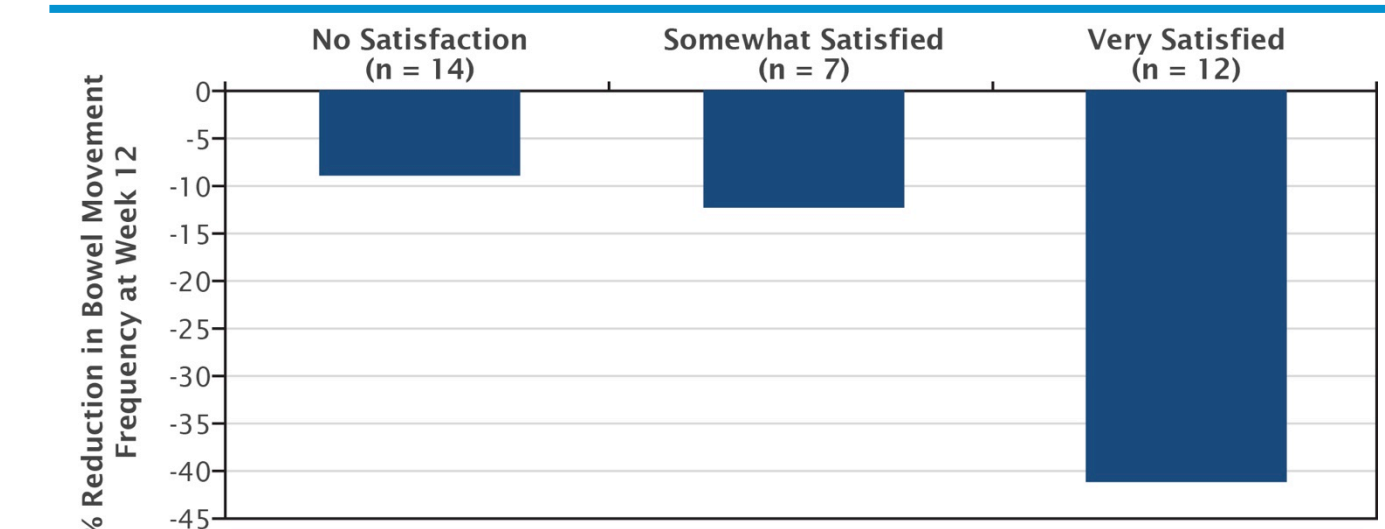
Symptom Improvement	Frequency of Reports in Patients Who Reported Any Symptom Improvements n (%)
Too frequent BMs	21 (88)
Stool consistency	19 (79)
Urgent BMs	14 (58)
Energy	12 (50)
Flushing	8 (33)
Problems sleeping	5 (21)

Note: Table includes only symptom improvements reported by at least 20% of interview participants. N = 24 from pooled treatment arms.

Quantitative Assessments

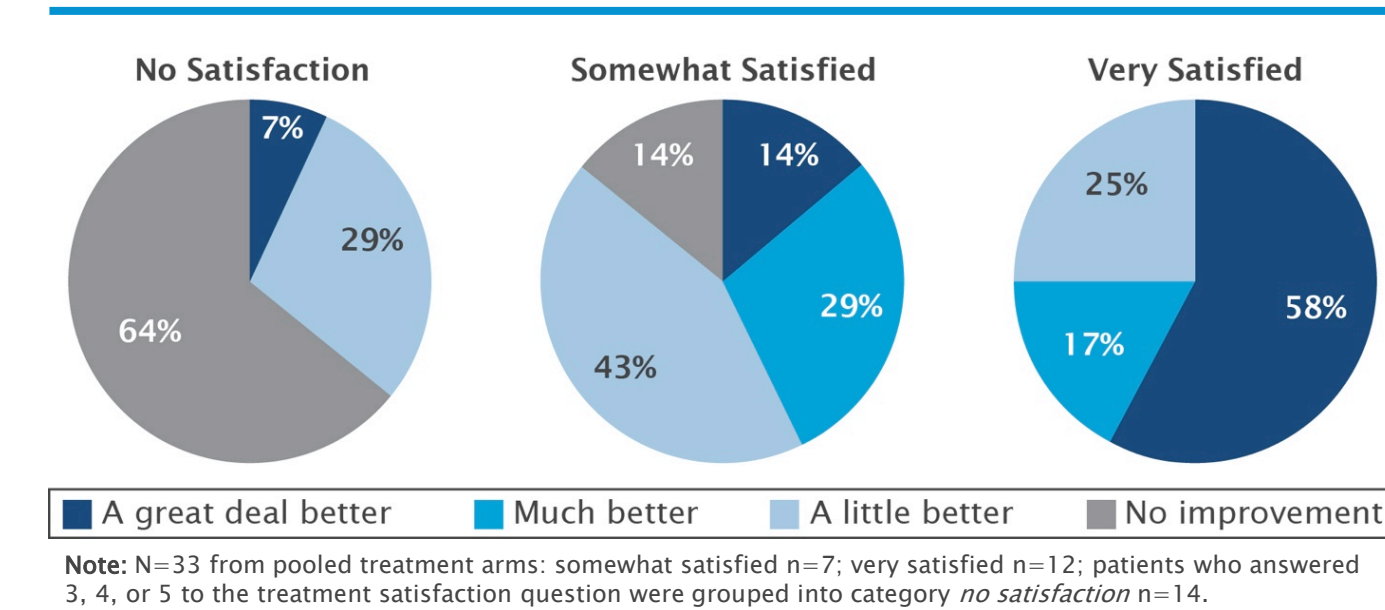
- Among the 33 participants (placebo:250:500 = 9:9:15) answering the interview question about treatment satisfaction (Question 3), 55% across all arms reported being somewhat or very satisfied with the treatment they received during TELESTAR.
- Patients with greater satisfaction reported greater reduction in BM frequency (Figure 1).
- A correlation (R = 0.66, P < 0.001) was seen between reported change in BM frequency question (Question 1) and treatment satisfaction (Question 3).
- Reports of very satisfied (interview Question 3) were 0% (0/9) on placebo (SOC) and 50% (12/24) on TE, with similar results in the 2 TE dosage groups.

FIGURE 1: Relationship Between Treatment Satisfaction and Percentage Reduction in BM Frequency at Week 12 (n = 33)



Note: Treatment satisfaction is reported in the context of the patient interviews (Question 3). BMs were reported daily on electronic diaries during TELESTAR. N=33 from pooled treatment arms. Patients who answered 3, 4, or 5 to the treatment satisfaction question were grouped into category no satisfaction.

FIGURE 2: Self-reported BM Frequency Improvement and Treatment Satisfaction (n = 33)



Note: N=33 from pooled treatment arms: somewhat satisfied n=7; very satisfied n=12; patients who answered 3, 4, or 5 to the treatment satisfaction question were grouped into category no satisfaction n=14.

Conclusions

- The primary endpoint of TELESTAR, a reduction in BM frequency, was very meaningful to patients.
- Effective reduction in BM frequency led to improvement in emotional well-being and social and physical function.
- The highest level of treatment satisfaction was reported only on telotristat etiprate, not on placebo.

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DISCLOSURE

Authors who are employees of Lexicon Pharmaceuticals, Inc. may own common stock or may have been granted stock options or other equity incentive awards. *Former employee; currently at BioHealthConsult, Cincinnati, OH.