

Carcinoid Syndrome - FDA-Requested Listening Session

April 27, 2023

Objectives of Session

To gain a better understanding of the experience of individuals who have or had carcinoid syndrome; the impact of symptoms on family, caregivers, and activities of daily living; what patients and their caregivers would consider a meaningful improvement in symptoms, and treatment preferences.

Discussions in FDA Listening Sessions are informal and not meant to replace, but rather complement, existing patient engagement opportunities in the Agency. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report summarizes the input provided by persons from the carcinoid syndrome community at the meeting. To the extent possible, the terms used in this summary describe the health needs, perspectives, preferences, and impacts reflect those of the individual participants. This report is not meant to be representative of the views and experiences of the entire carcinoid syndrome population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

Participants Represented

- **Number of Participants:** Five
 - Four participants living with carcinoid syndrome; two females and two males
 - One participant was a caregiver for a patient living with carcinoid syndrome.
- **Ages:** Participant ages ranged from 38-77 years of age.
- **Education level:** Participants' self-reported highest level of education ranged from high school diploma to master's degree.
- **Health literacy:** Participants' level of self-reported health literacy ranged from average to above average.
- **Geographic location:**
 - Three participants were from the Southeast, United States (U.S.).
 - One participant was from the Midwest, U.S.
 - One participant was from the West, U.S.
- **Disease Severity:** Participants' self-reported severity of carcinoid syndrome ranged from 2 (have symptoms, but do not require adjustment to daily activities) to 4 (daily activities require adjustments > 50% of the day).

Summary of Discussion by Question

Round 1: Symptom Management

1. **Of all the symptoms that you have experienced because of carcinoid syndrome, can you tell us which 1-2 symptoms are most bothersome to you?**

Please describe the symptoms, including how often they occur and how severe they are. Are there specific triggers you have identified that cause your symptoms to occur, or to increase?

- Two participants shared that flushing and diarrhea are the symptoms most bothersome to them.
 - One participant named flushing episodes as their most bothersome symptom.
 - One participant mentioned that fatigue causes them more discomfort than most other symptoms, but flushing would be another symptom.
 - Another participant indicated that diarrhea and nausea are the most bothersome symptoms.
 - Two participants and a caregiver participant described flushing episodes as random and unpredictable in severity. Another participant said that their flushing occurs when swallowing liquids.
 - All but one participant who listed diarrhea as bothersome shared that what they eat and drink can trigger their symptoms.
 - Two participants mentioned that they notice their symptoms tend to worsen in the days before their next dose of medication is due.
 - One participant shared that anxiety and stress act as triggers for symptoms.
- 2. Follow-up question: When you were speaking about specific triggers, and how something might trigger your symptoms, were you referring to something triggering flushing episodes in particular, or other symptoms?**
- One participant shared that a trigger could lead to any and all symptoms. They said that flushing is typically the first symptom to manifest before other symptoms, like diarrhea and nausea.
- 3. Follow-up question: Do your symptoms occur at the same time, one after the other, or in isolation?**
- Three participants said that they often have symptoms that will lead to other symptoms. They specifically noted that if they have diarrhea, they will almost certainly have a flushing episode or nausea.
 - A caregiver participant shared that their loved one's can experience multiple symptoms at the same time, or one symptom in isolation.
 - Another participant noted that their symptoms tend to present randomly.
- 4. Please describe how you currently manage symptoms of carcinoid syndrome, such as any medications or other lifestyle interventions that you have tried.**
- Several participants noted that they or the patient are taking lanreotide (also known as Somatuline Depot®) to “control tumor growth.
 - Four of the five participants shared that they use loperamide (also known as Imodium A-D®) to help with diarrhea.
 - One participant explained that they have started practicing Stoicism, taking trazodone, and participating in a cancer support group to help alleviate stress and anxiety.
 - Two participants mentioned ondansetron (also known as Zofran®) as a medication they take to combat nausea.
 - One caregiver participant shared that the patient controls their symptoms by using “rescue” short-acting octreotide (also known as Sandostatin®), in addition to lanreotide and telotristat ethyl (also known as Xermelo). Telotristat was reported to be used to “reduce serotonin.”
 - One participant said they take large doses of ibuprofen (also known as Advil® or Motrin®) for abdominal pain.

- Several participants noted using pain relieving medications including ibuprofen, oxycodone (also known as Oxaydo[®], OxyCONTIN[®], RoxiBond[®], Roxicodone[®], or Xtampza[®]), or morphine (also known as Arymo ER[®], Kadian[®], MorphaBond[®], or MS Contin[®]).

Round 2: Quality of Life

5. How much of an impact do symptoms of carcinoid syndrome have on you? This could include how the symptoms impact your ability to do certain tasks that are important to you, or how you feel it impacts the overall quality of your life. Please describe the impact on you personally; if symptom(s) also impact your family, caregivers, or others, please comment on that aspect as well.

- Three participants stressed how carcinoid syndrome has impacted their lives when it comes to using the restroom. All three noted that they now must be aware of the location of the nearest bathroom wherever they may be.
- Two participants shared that carcinoid syndrome has impacted their relationships with loved ones. One participant expressed concern that they sometimes lose their temper or experience “fits of rage” and lash out at their spouse, and they feel embarrassed afterward to have acted this way toward others. Another explained that their partner has secondhand stress about the potential of a carcinoid syndrome flare-up.
- A caregiver noted that carcinoid syndrome has completely changed the life of their loved one to the point that they are no longer able to do many of the things they loved. Sometimes their loved one is barely able to walk due to symptoms. Symptoms require them to be flexible as how he feels may change dramatically day to day and so it is difficult to make plans in advance.
- Two participants noted that they cannot stand up for long periods of time, due to fear of passing out.
- Two participants noted that they had to stop working due to the disability associated with their carcinoid syndrome symptoms.

Round 3: Potential Treatments

6. If you were to take an effective medication to control carcinoid syndrome symptoms, what would be the first and most important symptom you would want to improve or treat? In what ways would you want the medication to change your symptoms?

- Two participants shared that they would like an effective medication to control diarrhea. Both shared that outside of completely eliminating the symptom, they would like a medication to lessen the impact, such as the urgency.
- A participant and a caregiver participant both said that a medication to control flushing would have a great impact. The caregiver participant noted that flushing often seems to trigger additional symptoms; thus, a medication that could either stop flushing, or delay it, even if for a short period of time would be helpful.

- Another participant shared that fatigue would be the symptom they would most like to have controlled.

7. Follow-up question: What aspect of diarrhea is most bothersome to people?

- All the participants said that urgency is the most bothersome aspect of diarrhea. They all stressed how quickly diarrhea comes on and how there's little that can be done once it occurs.
- One participant noted that after urgency, frequency of diarrhea is the next biggest issue, as they have to use the bathroom many times per day.

8. Follow-up question: What does it feel like when having a flushing episode? Are you always aware it's happening?

- One participant shared that flushing feels like a burning sensation or "hot internally" and presents with blotchiness on the skin. They also noted their eyes tend to get bloodshot.
- Another participant explained that they were flushing at the time of the listening session.
- The participants said that in the past they had episodes where their entire body turned pink and it was apparent to others.
- A participant and a caregiver participant both noted that the flushing episodes have gotten to the point where minor episodes often don't manifest externally so it can be difficult to tell when flushing is happening.

9. Follow-up question: Can you describe your abdominal pain? Is it colicky, distension, stabbing? How do you get relief from the pain?

- Two participants shared that the pain presents as a deep ache. A caregiver participant shared that their spouse experiences pain that he describes as "right above the liver."
- A participant explained that their abdominal pain can be described as colicky, as it is usually a result of extreme bloating from diarrhea. They also noted they have liver pain but believe that is due to a liver that functions at 30%.
- A participant said that they take large doses of ibuprofen (also known as Advil[®], Motrin[®]) for pain, and on occasion take oxycodone (also known as Oxaydo[®], OxyCONTIN[®], RoxiBond[®], Roxicodone[®], or Xtampza[®]) if the pain is too severe.
- Another participant noted that they have a fentanyl (also known as Durogesic[®] or Ionsys[®]) patch they apply to help ease abdominal pain.

10. Follow up question: Do some of your complex symptoms occur at night to the point where you are awakened?

- Three participants explained that they have night sweats and/or hot flashes. One stated that they are unsure if those are directly related to carcinoid syndrome but noted that the sweating began occurring after diagnosis.
- A caregiver participant said that their spouse often wakes up 2-3 times in the middle of the night to have a bowel movement.
- Another participant explained that they have less symptoms at night, and they feel this is most likely because lying in bed offers less opportunities for stress to trigger symptoms.

11. Would you consider taking a potential medication that decreases the severity of a carcinoid syndrome symptom, rather than completely resolving it? Why or why not? If yes, how much

would your symptoms need to improve, so that you would consider it to be beneficial to keep taking the medication?

- Four of the five participants said that they would consider taking a potential medication that decreases severity of a symptom, because they would welcome any amount of improvement.
- One participant explained that they would like a medication that controls metastatic growth of their cancer in other organs.
- Another participant noted that they would like a medication that reduces the effect of triggers.
- Two participants shared that they would take a potential medication as long as the side effects weren't more severe than the symptoms.

12. Follow-up question: Regarding your desired improvement in flushing, could you describe what type of improvement would be meaningful for you? For example, having fewer episodes, less severe episodes, episodes of shorter duration? What type of improvement in your symptoms of flushing do you have in mind?

- One participant explained that any improvement regardless of what improved and how much would be helpful. They noted that the severity of their flushing episodes is so varied that it's hard to predict how much a medication could help.
- A caregiver participant said that an improvement in the severity of their spouse's flushing episodes would be welcome. They also said they would appreciate if a medication could limit the flushing episodes that come in clusters (such as flushes that last ~30 seconds, but may have 10 within a 15-minute window).

13. Follow up question: What aspect of diarrhea would you hope a medication would initially target?

- Three participants stated that urgency is the most pressing issue related to diarrhea.
- One participant noted that after urgency, reducing the number of stools per day would be their next priority.
- One participant noted that the consistency of the stool is not important to them.
- Additionally, two participants noted that the impact of diarrhea leads them to often go without eating all day, out of worry of experiencing diarrhea.

FDA Offices & Divisions in Attendance

- **Office of the Commissioner (OC) – 4 offices**
 - OC/OCPP/PAS – Office of Clinical Policy and Programs/Patient Affairs Staff (*organizer*)
 - OC/OCE – Oncology Center of Excellence
 - OC/OCPP/OOPD – Office of Clinical Policy and Programs/Office of Orphan Products Development
 - OC/OCPP/OCPR – Office of Clinical Policy and Programs/Office of Combination Products
- **Center for Biologics Evaluation and Research (CBER) – 2 offices/divisions**
 - CBER/OCD – Office of the Center Director

- CBER/OCD/PS – Office of the Center Director/Policy Staff
- **Center for Devices and Radiological Health (CDRH) – 7 offices/divisions**
 - CDRH/OPEQ/OHTI/DHTIB – Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology I B
 - CDRH/OPEQ/OHTI/DHTIC – Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology I C
 - CDRH/OPEQ/OHTIII -- Office of Product Evaluation and Quality/Office of Health Technology III
 - CDRH/OPEQ/OHTIII/DHTIIIB – Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology III B
 - CDRH/OPEQ/OHTIII/DHTIIIC – Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology III C
 - CDRH/OPEQ/OHTIV/DHTIVA - Office of Product Evaluation and Quality/Office of Health Technology IV/Division of Health Technology IV A
 - CDRH/OPEQ/OHTVIII B - Office of Product Evaluation and Quality/Office of Health Technology VIII B
- **Center for Drug Evaluation and Research (CDER) – 8 offices/divisions**
 - CDER/OND/OII/DG – Office of New Drugs/Office of Immunology and Inflammation/Division of Gastroenterology
 - CDER/OND/OCHEN/DCN – Office of New Drugs/ Office of Cardiology Hematology Endocrinology and Nephrology/Division of Cardiology and Nephrology
 - CDER/OND/ODES/DCOA – Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment
 - CDER/OND/OOD/DOII – Office of New Drugs/Office of Oncologic Diseases/Division of Oncology II
 - CDER/OND/ORDPURM/DRDMG – Office of New Drugs/ Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/ Division of Rare Diseases and Medical Genetics
 - CDER/OND/OSM/DIRM – Office of New Drugs/Office of Specialty Medicine/Division of Imaging Radiation Medicine
 - CDER/OTS/OB/DBII – Office of Translational Sciences/Office of Biostatistics/Division of Biometrics II
 - CDER/OTS/OB/DBIII – Office of Translational Sciences/Office of Biostatistics/Division of Biometrics III

Non-FDA Attendees

- Reagan-Udall Foundation for the FDA
- National Organization for Rare Disorders
- National Institute of Health

Financial Interest

Participants did not identify financial interests relevant to this meeting and are not receiving compensation for participation in this listening session.