

# **Primary Biliary Cholangitis (PBC) Externally-Led Patient-Focused Drug Development (EL-PFDD)**



TITLE: Global Liver Institute Primary Biliary Cholangitis (PBC) Externally-Led Patient-Focused Drug Development (EL-PFDD)

CO-AUTHORS:

Donna Cryer, CEO & President, Global Liver Institute

Daniel Nam, Vice President, Policy, Global Liver Institute

Royze Cachero, Program Manager, Pediatric and Rare Liver Diseases, Global Liver Institute

Robert Mitchell-Thain, Chairman of GLI's Pediatric and Rare Liver Diseases Council

*With the support of Christine Maalouf, Lily Benig, Anna Lin, Chloe Kim*

COLLABORATORS:

University of Milano-Bicocca (Marco Carbone); University of Miami (Cynthia Levy); PBC Foundation (Colette Thain); EASL; PBCers (Carol Roberts); Canadian PBC Society (Gail Wright); Dr. Joseph Turner, Bettina E. Hansen; Bob Tyler, Lavinha Ashanti, Richard Cook, Leslie Stratta, Mo Christie, Doreen Donaldson, Deb Sobel, Danielle Cleary, Angela Eddy, Donna Boll, Cathy Mumford

DISCLOSURES: There are no disclosure interactions by any of the authors, or contributing organizations, that are relevant to this resource.

FUNDING RECEIVED OR GRANTED: External funding was not accepted for the PBC EL-PFDD meeting.

VERSION DATE: October 28 2022

This document has not been revised and/or modified in any way after the version date listed above.

Global Liver Institute (GLI) gives the FDA the necessary permissions to link this resource from the FDA website, and the posting of this resource will not violate the proprietary rights of others.

# Contents

## **1. BACKGROUND**

EL-PFDD Overview and Objectives

## **2. MEETING OVERVIEW**

Collaborators and Attendees

Key Findings

## **6. PANEL I**

General Theme: Clinical Features of PBC –  
how does PBC affect my life?

## **12. PANEL II**

General Theme: Current Therapeutic  
Approaches – How does the current  
therapeutic landscape affect my life?

## **18. Panel III**

General Theme: The Future of Clinical Trials –  
How can we design an ideal clinical trial?

## **22. SURVEY RESULTS AND FINDINGS**

### **23. SURVEY HIGHLIGHTS**

Disease State and Symptoms Questions

Treatment Questions

Demographic Questions

### **36. BIOS**

### **40. CONCLUSION**

### **42. APPENDIX**

Meeting Agenda

Patient Survey on Benefits and Risks  
of Potential Treatments for PBC

# Background

Global Liver Institute (GLI) is a patient-driven 501(c)3 nonprofit organization headquartered in Washington, DC, with offices in the EU and UK, founded in the belief that liver health must take its place on the global public health agenda commensurate with the prevalence and impact of liver disease and the importance of liver health to well-being. GLI promotes innovation, encourages collaboration, and supports the scaling of optimal approaches to improve research, care, and policy. By bringing together more than 200 community-based, national, and international organizations across its councils, campaigns, and events, GLI equips advocates to identify and solve the problems that matter to liver patients. With the goal of informing and driving forward the next generation of clinical trials and treatment approvals, GLI and the liver patient advocacy community held a PBC EL-PFDD meeting on **February 4, 2022**.



## Primary Biliary Cholangitis Overview

Primary biliary cholangitis (PBC) is a chronic, rare, autoimmune disease of the liver that slowly destroys the medium-sized bile ducts, eventually causing cholestasis (disruption of the bile flow), cirrhosis (scarring and deterioration of liver), and liver failure. It was formerly known as primary biliary cirrhosis.<sup>1</sup>

PBC has an unclear etiology. Although relatively rare, PBC is the most common liver disease associated with chronic cholestasis in adults, with a prevalence of about 39.2 per 100,000 inhabitants.<sup>2</sup> The highest prevalence of cases are found in adult women: Approximately 95% of cases occur in women ages 35 to 70,<sup>3</sup> and 90% of all cases are women.<sup>4</sup>

The most common symptoms of PBC are fatigue and pruritus, or severe itchy skin. Other symptoms include dry eyes and mouth, collection of fatty deposits in the skin around the eye, and pain in the joints, muscles or bones. Symptoms may vary in severity and might not correlate with the degree of liver damage in a patient.<sup>5</sup> Though there is currently no cure for PBC, current studies are concerned with developing therapies for both disease and symptom management.<sup>6</sup>

1. Leighton, J., Thain, C., Mitchell-Thain, R., Dyson, J. K., & Jones, D. E. (2020). Patient ownership of primary biliary cholangitis long-term management. *Frontline Gastroenterology*, 12(5), 370–373. <https://doi.org/10.1136/flgastro-2019-101324>.

2. Lu, M., Zhou, Y., & Haller, I.V., et al. (2018). Increasing prevalence of primary biliary cholangitis and reduced mortality with treatment. *Clinical Gastroenterology and hepatology*, 16(8), 1342-1350. <https://doi.org/10.1016/j.cgh.2017.12.033>.

3. Lee, T. H., & Peters, J. J. (2022, Jan). Primary Biliary Cholangitis (PBC). Merck Manual. <https://www.merckmanuals.com/professional/hepat-ic-and-biliary-disorders/fibrosis-and-cirrhosis/primary-biliary-cholangitis-pbc>.

4. Smyk, D. S., Rigopoulou, E. I., Pares, A., Billinis, C., Burroughs, A. K., Muratori, L., Invernizzi, P., & Bogdanos, D. P. (2012). Sex differences associated with primary biliary cirrhosis. *Clinical and Developmental Immunology*, 2012, 1–11. <https://doi.org/10.1155/2012/610504>.

5. NHS. "Primary biliary cirrhosis." NHS, 2021, <https://www.nhs.uk/conditions/primary-biliary-cirrhosis-pbc/>. Accessed 17 Aug 2022 August 2022.

6. Chascsa, D. M. H., & Lindor, K. D. (2020, January 22). Emerging therapies for PBC - *Journal of Gastroenterology*. SpringerLink. Retrieved August 17, 2022, from <https://link.springer.com/article/10.1007/s00535-020-01664-0>.

# Meeting Overview

The PBC EL-PFDD meeting marked the continuation of productive hepatology conversations that the liver advocacy community has had with the U.S. Food and Drug Administration (FDA) throughout the past years. **Clinical and patient experts joined GLI to discuss current unmet needs of PBC patients, and to provide the FDA and other relevant stakeholders with a wide range of patient and caregiver input on PBC.** These insights included various perspectives on the condition, including its impact on daily life, future therapy risk and benefit tradeoff, and the urgency around developing therapies.

## Collaborators and Attendees

To ensure the success of the event, GLI collaborated with other liver patient advocacy organizations (e.g., PBC Foundation, PBCers, Canadian PBC Society) and leaders in the PBC community on survey development, dissemination, promotion, and patient/caregiver participation. Additionally, GLI was able to gather a wide spectrum of leaders outside of the liver patient community at the event, including from multiple divisions from the FDA and other institutions.

With more than 160 stakeholders attending the meeting virtually, their input reflected a diverse set of experiences with the symptoms and treatments for this disease. The archived webcast is available to watch at [https://youtu.be/Z2c\\_G-hPVw0](https://youtu.be/Z2c_G-hPVw0).



## Key Findings

This PBC EL-PFDD outcome report provides an overview of the PBC EL-PFDD meeting that occurred on February 4, 2022. **The report summarizes the input shared by panelists and attendees during the meeting and includes an analysis of the results from the PBC survey.** The terms used in this report to describe PBC symptoms, impacts, and treatment experiences reflect the words used by the meeting attendees or survey commenters. There may be symptoms, impacts, treatments, or other aspects of PBC that are not included in this report.

The input from the meeting and survey comments provided rich detail on the impact that PBC has on patients, caregivers and family members. **Participants highlighted the physical, emotional and social toll PBC takes on daily life and focused on the need for new treatment options.** The following are several key findings summarized from these discussions.

- Patient support groups have a significant impact on participants' quality of life, as these groups are avenues for learning about their disease, finding emotional support, and connecting with other advocates and newly found friends.
- Registries allow patients to take control of their health through consensual data sharing. Most patients receive a late diagnosis due to misinformation and lack of education, rather than negligence.
- Patients desire more research and clinical trials on new medication for symptom prevention, specifically for fatigue and itching. Participants revealed that there are various unmet needs that cannot be addressed directly by hepatologists and clinicians due to the lack of standardized measurements.
- Current therapeutics like ursodeoxycholic acid (UDCA) and obeticholic acid (OCA) for PBC, in addition to synthetic controls, act as alternative options for placebos in clinical trials for quicker and more efficient results.
- Hematologists and clinicians cannot directly address some of the needs of patients such as work-life balance, fatigue, and itching. Thus, participants looked to patient advocacy organizations for assistance.
- Conversations on the different aspects of health management are crucial in order to encourage patients to make changes to their lifestyle by addressing nutrition, mental health management, and stress.
- For future clinical study design, participants suggest that researchers keep patients in mind as they create entry criteria, determine ethics for placebo randomization, and lower endpoint risk for disease-modifying drugs and Quality of Life Scale, or QOLS (particularly liver stiffness as a new endpoint measurement), and that they involve patients as early as possible. Good research design involves patients as collaborators.
- Common barriers to clinical trial participation are distance, limited accommodations, and inaccessibility. Patients suggest the use of telehealth as a solution to these barriers, but drawbacks to this approach include challenges with randomization, follow up, and other specifications.
- Real world data can be used as an external control to treat patients as it describes the natural history of the disease, identifies the risk factors, provides post-marketing surveillance, and acts as a comparison with treated patients. These benefits contribute to the willingness, transparency, and trust in the information presented to patients.



# Panel I

## General Theme: Clinical Features of PBC – How does PBC affect my life?

**The first panel focused on discussing the foremost symptoms associated with PBC.** During this section of the meeting, the audience heard directly from the panel about the impact of their disease on everyday life events, such as work, family, and daily activities. The panel also expanded on how PBC impacts their quality of life.

The conversation was moderated by the Chairman of GLI's Pediatric and Rare Liver Diseases Council, Robert Mitchell-Thain, and included six panelists who represented a variety of segments within the patient community and highlighted the diverse impact of PBC.



## The panel included:

### **Bob Tyler,**

a patient who was diagnosed with PBC and autoimmune hepatitis (AIH) 9 years ago

### **Levinia Ashanti,**

a patient who was diagnosed with PBC in 2018

### **Richard Cook,**

a patient who was diagnosed with PBC in 2019 shortly after a bad fall and a subsequent diagnosis of osteoporosis

### **Leslie Stratta,**

a patient who was diagnosed with PBC in 2017

### **Carol Roberts,**

a patient diagnosed with PBC in 1999

### **Mo Christie,**

a patient diagnosed with PBC in 2017

---

The panelists' statements provided a vivid depiction of the burden of PBC on many aspects of daily life, indicating that fatigue, itching, and general pain most impacted their lives. **In particular, panelists spoke of the debilitating pain and fatigue that rendered everyday activities nearly impossible.** They also shared the physical impacts of fatigue and pruritus on their bodies. Although key symptoms were discussed, panelists also each emphasized their own unique complications as a PBC patient.

Patients also discussed the social consequences of their symptoms – the very real effects on their personal, family, and community lives. In the face of such debilitating symptoms, many expressed concerns with the inevitability of disease progression and the toll that countering symptoms without a cure takes on their mental and physical health.

## Some of the key comments from the panel discussion are listed below:

### Bob Tyler

“I have 5 grandchildren with 2 more on the way, ranging in age from one to fifteen years old. Not only do I have to, I want to, as the grandfather, get on the ground with the little ones and play. I want to play catch with the older ones. They have games and events in their lives that I don’t want to miss. But it’s hard because this pain truly controls my everyday life. This is sad to say, but I have to be honest: I truly feel that the pain that I experience throughout my body is going to kill me faster than PBC or AIH ever will.”

“The medicine seems to be doing its job slowing the progression down. What isn’t slowing down, though, is the pain and fatigue.”

“This pain, there is nothing. There’s no therapy to make it better, there seems to be no light at the end of the tunnel. **We need help to manage this pain.** To control the fatigue that involves our everyday lives. I tell people that I am almost 64, but I look 74 and I feel 84. I’m not asking to feel like a kid again, but the pain more so than the fatigue affects me mentally as well as physically. We need your help.”

### Levinia Ashanti

“It’s been a struggle. I’ve gained a lot of weight. I’ve lost a lot of hair so I have to wear wigs and extensions. I feel drowsy and sleepy. I struggle with vomiting, bleeding. I can’t always leave the house on my own. Just to go shopping, I find it overwhelming. I get snappy and very irritated. It’s hard to pinpoint whether it’s because of the PBC or the medication themselves.... PBC affects me emotionally, just not being able to do stuff on my own anymore, having to constantly rely on others. Your confidence goes, and it’s really challenging... **My mental health deteriorated over this diagnosis.**”



“People don’t really understand the disease. So without sympathy or empathy for you, they think you’re just overreacting or being too sensitive. I am slowly trying to get back into a place where I feel comfortable to do things with my daughter again. Taking baby steps, I hope by the end of the year I’ll be able to go back to work. But the pain does affect everyday life. And it’s hard to function. And there’s not much you can do to get rid of it.”

## Richard Cook

“I have lived a lifetime of physical activity, including recreational basketball and power walking and weight training. As an adult, I earned the black belt in karate. I tell you these things to contrast my earlier lifestyle with my condition now. During the past four years, I’ve had a significant decline in my physical health. I’ve lost 20 pounds in muscle mass and my loss of strength has been dramatic. I climb stairs with difficulty because of leg weakness, and I struggle with balancing and my energy levels have flagged. I need to rest more now and I have been more restricted in the activities I can do.”

“I live with my disease and accept its symptoms, but I have lingering concerns about PBC’s progression and how much more limiting my symptoms may become. **I am thankful for the research being done on PBC and for the therapeutics being done in this area.** I don’t expect a cure or solution to the symptoms during my lifetime, but I’m hoping the progression of PBC can be slowed or stopped for me and my fellow PBCers. And for younger generations to not have to suffer this disease.”

## Leslie Stratta

“I felt like I was forced to consider my mortality at the young age of 43... Having PBC has definitely humbled me. It has taught me that it’s okay to be vulnerable. It’s through that vulnerability that I’m called to patient advocacy, not only for myself, but for all of us trying to manage this confusing, everchanging autoimmune liver disease.”

“I had to educate myself and really understand what therapy means. **The goal is to stop the progression of the disease, and if this treatment would do that, the side effects are a risk I’m willing to take.** I’m grateful to say that I am responding to therapy, still relatively asymptomatic. The itching comes and goes, but I do have to monitor where that itching is coming from because I do have psoriasis as well. So I can’t always assume that the itching is from the PBC. What I make sure to do is take care of myself. I medicate, practice mindfulness, and keep my mental and emotional health in check. I have therapy and a wonderful group of PBCers that I can rely on when I am not feeling well. I watch my nutrition, and I make sure to build some kind of physical activity each day... I have to listen to my body. I have to listen to my mind. I have to make sure that I am not blaming myself or guilt myself into doing something I am just not physically capable of doing for that day.”

“There are moments when I start to question myself: Is my disease getting worse despite all my efforts? Am I becoming resistant to my second-line therapy? What if that happens? Is there going to be another treatment to help me? But the question that weighs the heaviest on me is: will I need a liver transplant? And while the ultimate goal is for a cure for PBC, I also hold onto the hope that patient focused drug development efforts can lead to interventions that can stop PBC disease progression. Because that is what is most critical for those of us who are truly to do everything we can to live with PBC.”

### Carol Roberts

“I went through severe itching, to the point that parts of my body looked like I went through a car crash because they were so bruised from my rubbing.”

“I worked for a company that had retail outlets and I wrote a check for \$87 to cover the rental space that should have been \$87,000. At that point I decided that it may be better for me to leave my job. And I was fortunate enough that I was able to do that. And being at home and living life as I needed to, resting when I wanted, getting up when I wanted, seemed to help. I started to improve as I went along.”

“I always felt like I was doing so well, but I didn’t want people to look at me and say, ‘well she can run around and do all this, so PBC must not be so bad.’ As a patient advocate for PBC, I always make sure that others get to see everyone else’s story as well.”

“By the end of 2020, my liver just tanked and along with it it took my kidneys. So in January, I spent every week in the hospital having paracentesis and they were removing 3-5 liters of fluid weekly. **By April, my kidneys were starting to crash and I was finally listed for transplant.** I was listed for transplant on May 1st and I was transplanted on May 6th... I received the transplant on Friday, and they told me I probably would not have seen Monday without the liver transplant.”

“Transplant is a wonderful experience when you need it, but it is not easy. Getting sick enough to need one and the shortage of donated organs is not the solution. I feel very fortunate that uracil slowed my liver disease progression for so many years, but what if there had been another treatment? Every PBC patient has a different journey, and because the theory is that you are genetically predisposed and something can trigger it to set it off. We don’t know what that trigger is. It may be different for each person. We



really need to look at many options for the patient. Until we find the cause of PBC, patients will need PBC treatments that work with their personal history and improve their quality of life. The patients are very grateful for companies looking into treatment of rPBC [recurrent PBC] and we appreciate their efforts in including patient voices in creating clinical trials and listening to what we need to do to improve our lives. We appreciate the FDA taking the time to hear all the patient voices and learn from us how PBC affects our lives and what we need.”

### **Mo Christie**

**“The itch was awful.** My skin was always bleeding and bruised. It always led to infections. I couldn’t sleep, which added to my fatigue and it was taking a huge toll on my mental health. I tried lots of medication, some of which had very bad side effects... My quality of life was very poor at this point. I was too sore and tired to spend any time with my family. I worked through all the treatments again, but nothing worked. I was reassessed for transplant, by which point my quality of life deteriorated further.”

“I know some people may find it difficult to understand why I chose a liver transplant simply because of itchy skin, and I see their points. I was the same. But the itch associated with PBC is brutal, and we desperately need a treatment for the itch. I agree transplant should not be considered the only treatment for that.”

# Panel II

## General Theme: Current Therapeutic Approaches – How does the current therapeutic landscape affect my life?

**The second panel focused on the current therapeutics available to PBC patients and their experiences.** The panelists examined the debilitating effects of PBC symptoms and explored available treatment options for effective disease management. Panelists discussed their experiences with their healthcare system and underlined the role of social support in disease management. Some discussed the social stigma associated with liver disease, especially for minorities, underrepresented communities, and historically vulnerable communities.

The conversation was moderated by the Chairman of GLI's Pediatric and Rare Liver Diseases Council, Robert Mitchell-Thain, and included five panelists.



## The panel included:

### **Doreen Donaldson,**

a patient diagnosed with PBC diagnosed in 1988

### **Gail Wright,**

president of Canadian PBC society, PBC patient, and PBC patient advocate

### **Deborah Sobel,**

a patient living with an autoimmune disease that has targeted her liver for the past 30 years

### **Danielle Cleary,**

a patient diagnosed with PBC with AIH overlap in 2020

### **Collette Thain,**

a patient and patient advocate who has been living with PBC for 25 years

---

The panelists summarized currently available therapies for PBC. **They discussed their personal visions for objectives of PBC therapeutics, including the importance of symptom management and prevention of disease progression.** Several panelists stressed the importance of continued research and development to create more effective treatments for fatigue, pruritus, and other physically taxing symptoms. In addition, panelists shared how social support is vital in navigating the therapeutic landscape for PBC, with many highlighting the sense of stigmatization, isolation, and despair that often accompanies a PBC diagnosis. Some underlined the importance of listening to patient voices to address patient-focused priorities when developing novel therapeutics.

## Some of the key comments from the panel discussion are listed below:

### Doreen Donaldson

“The fatigue is something that you can’t overcome. Even if you get a good night’s sleep, if you happen to have one, you’re still fatigued the next day. What really bothered me was when friends and family cannot accept that the fatigue makes it so that you can’t be bothered to go out. When I was younger, I would pack the camper van to go camping. But by the time [it was unpacked], I was too tired to go anywhere so my husband used to have to unpack it again.”

“I wish there was more research into fatigue and if there is anything that could help. I know that the members here in Australia feel isolated because we don’t have the support network that people in the US, UK, and Scotland have. And I do try to get people together before COVID. We used to have pockets of people meet face to face, people who knew what it was really like to go through PBC. Because to an ordinary person, you look so well. But people don’t understand what is going on inside: how fatigued you are... If something could be done for the fatigue, especially for the young ones, I hope one day, there may be something to help with fatigue. **And I hope one day, there may be a cure for PBC.**”

### Gail Wright

“While most PBC patients feel the stigma of liver disease, First Nations PBC patients face the added burden of overcoming discrimination and stereotypes of substance abuse and alcoholism. Patients feel that they were made to feel that PBC was somehow their fault and they felt frustrated that their reported symptoms were often trivialized. [First Nations] PBC patients also lack meaningful and accessible resources, which can weaken language barriers that foster a culture of distrust. Barriers to treatment are lack of disease awareness among health care professionals and limited number of specialists in remote and rural communities. Understanding the patient’s lived experience helps us understand how a treatable disease like PBC can lead to suffering, poor outcomes, and miscommunication in our communities.”

**“I think it’s important to add that patients that face discrimination are more likely to be misdiagnosed or diagnosed at advanced stages.** Therefore, it increases the likelihood of adverse outcomes... While First Nations PBC patients face unique challenges, they have much in common with all PBC patients. I believe they also represent voices that are often not represented in discussion regarding patient outcome and treatment experiences.... There is much work to be done to change current attitudes and practices to ensure that marginalized and vulnerable populations are included in all discussions regarding the health of their communities.”



## Deborah Sobel

“For me, ‘scattered’ is the perfect word to describe autoimmune disease and the related treatment. It goes everywhere, it hardens everything. The degree with which it shows up as a problem or not depends on what it is targeting. The treatment is scattered, with each specialist each focusing on their own area of speciality: bone marrow, salivary glands, liver. Scattered.”

“Regulators are scattered also. Regulators address symptoms as they present, but not the core problem. There is no captain on our metaphorical medical ship. Why is the body attacking itself? The scattered approach to the patient leads to multiple specialists, multiple PAs, and multiple ideas of what treatment should be. Patients end up being identified as hypochondriacs because they continuously come back with more issues and more problems. What have I earned as a result of this scattered approach? Diagnosis is a long process, extended because the patient is not having the core problem labeled correctly. We loathe to complain and say more is going on. Even after I identified that my body was attacking itself, I was treated as a liver patient. New symptoms were not responded to correctly. Patients and their voices demand more respect in the process. They should be referred to as equal partners. New treatment is vital, especially as related to autoimmune disease. We are mostly treating symptoms. We need to address the core issues. We need to be heard throughout the drug and treatment approval process. No final decision on treatment should be made without patients. The core issue is something only they and they alone can speak to in a compelling way.”

“I think there is nothing more important for patients than patients coming together to talk about what is going on with them. When patients come there, there’s a kind of synergy and energy that happens. We share ideas. We might not be able to fix the problem, but the loneliness that goes along with thinking that you’re the only one – that goes away. Anytime that you want to scream, shout, you know what you have listening and supportive ears. That is so powerful.”

## Danielle Cleary

“I was initially connected with a hematologist. However, she did not understand my case. I was put on a high dose of steroids. My liver enzymes were going down but not significantly enough. I took it upon myself to do some research and found a doctor with more experience with more difficult cases. The steroids were brutal. They have many negative side effects. I felt like my skin was burning. I felt like I had no control over my emotions, which was very hard on me and my family. I was very very hyper or not. It was just awful. My number one goal was to get off steroids, and I am very thankful for my doctor that I was able to do that... I really want to implore patients who are listening to be your best advocate and get there and try to find a doctor that is suitable for you. Because it is a rare disease, it is really upon us as patients, to advocate to get the best help that we can get.”



“I found out that a lot of people of Latinx descent and other people of color don’t typically respond well to the initial medication for AIH and PBC. This was very concerning to me and I brought it up to lots of people. I really implore that more research be done on this group of people, minorities and people of color, who are suffering and not responding as well to traditional therapies. This is a rare disease, and we are more rare even within this rarity. I understand that there are not a lot of ways to do studies, because we are such a small population. But I truly believe that we all deserve quality of care, quality of life, and best treatment that can be given.”

### **Collette Thain**

“I set out to inform people, to find people, and to support people. Anything I have I wanted to share with other people. [My hepatologist and I] created weight charts so people can keep track of their weight. But we wanted to not only help with simple physical things, but also the emotional side of things – the difficulties in living with PBC while trying to go about your daily life. And it’s frightening.”

“There is a movement in this country to start screening for lung disease. Let’s get it done for liver disease also. Some believe that all people under the age of 35 should receive a random liver function test. We should talk more and share our experiences. The medics are on our side. Pharma is out there. They know they can help us, and they have helped us. I believe we can help each other, stick together, and talk to each other. We’ve got good people on this side.”

# Panel III

## General Theme: The Future of Clinical Trials – How can we design an ideal clinical trial?

**The third panel focused on ideal clinical trial designs for patients, barriers to clinical trial participation, and patient perspectives on clinical trials.** The panel elaborated on the most impactful symptoms of PBC that should be addressed through clinical trials. However, many believed these could not be evaluated due to restrictions in current clinical trial designs. Some panelists discussed the importance of mutual understanding between key healthcare stakeholders and the PBC patient community. The panel also discussed involvement of patients in the clinical trial designing process.

The conversation was moderated by the Chairman of GLI's Pediatric and Rare Liver Diseases Council, Robert Mitchell-Thain, and included three panelists.



## The panel included:

### **Angela Eddy,**

a patient who was diagnosed with PBC 12 years ago and received a liver transplant 2 years after the initial diagnosis

### **Donna Boll,**

a patient diagnosed with PBC at the age of 35 after 5 years of investigation and 9 liver biopsies

### **Cathy Mumford,**

a patient who was diagnosed with early stage I PBC in 2006

---

The panelists' statements provided a vivid depiction of the burdens of PBC and the issues with getting appropriate treatments. **They highlighted the failure of current research methodologies to holistically and accurately evaluate the clinical impacts of PBC in patient lives.** Panelists suggested that incorporating more holistic measures to render the complexities of PBC should be the primary focus of clinical trials. They also underlined the importance of incorporating patient voice in the clinical design process.

## Some of the key comments from the panel discussion are listed below:

### **Angela Eddy**

“Most of the clinical trials involved questionnaires. They tended to be very closed questions or used Likert scales and visual analogues that evaluated outcomes on a draggable scale. And I just find that it reveals how scientists are focusing on collecting massive amounts of data and reporting on a wider scale. I personally find that to be very arbitrary. When you are trying to evaluate quality of life and impact

on things, it's quite difficult to evaluate by asking people to mark on a grid or answer on a greyscale. I often feel that information about quality of life requires a much more in-depth investigation. It's about the methodology and method. For me, I think it would be beneficial to see open-ended questions, semi-structured interviews, or focus groups and the like. It would enable a deeper look into what it's like to live with PBC... [Living with PBC] is a very complex picture. And we cannot simplify it into different scales. This may not be conducive to collecting a lot of data very quickly. But I think the world would benefit from the opportunity to study outcomes from a more in-depth and appropriate methodology for PBC patients."

"What are the way that we can capture PBC's effects? Personally, I would like to see that patients could be co-designers in the research design process. We need direct input from the PBC community. The acceptability of interventions or outcomes must be derived from patient preferences—thinking about what patients would like to see and implementing that in the study. It is also about using the right tools at the right time in the patients' journey. I was diagnosed with PBC 12 years ago, and I still get the same questionnaire 12 years later. That to me demonstrates how current evaluations use a lot of measures that are just not relevant or applicable anymore. We need to design new and innovative approaches that are specific to the PBC community. I also think we can learn from the pandemic. There are lots of opportunities now to use electrical devices, webinars, and self-reporting through electrical devices. This shift towards convenience can break down many patient barriers to make participating in clinical trials more accessible."

## Donna Boll

"I've suffered with PBC for 20 years. But never within those 20 years did I receive a single piece of information about PBC. Not one pamphlet. No support groups. I was, however, given the laughable amount of 3 bags of Urso. I want to talk about the cost of Urso for a moment. This is the first line of treatment. And everyone of the hundreds of thousands of people who have PBC do take Urso, often for 20 to 30 years. But prices literally range from \$15 per month to \$450 per month, for someone who pays cash. Why do costs vary so greatly between insurance companies and pharmacies? And when we only have this one choice, it's very scary to think that our lives depend on Urso. One single drug. We need more choices. When I asked what I needed to address today, one member in my support group said that there **needs to be a cure drug, not just one that delays progression**. The progression, even though it may be slow, is always in the back of the mind. I also want to discuss the quality of life affected by Urso. The itching it causes is unbearable. And this cost is prohibitive for many. People often talk about losing themselves or not feeling like they were going to be the same person they were. We are truly changed after having PBC. and our lives are changed forever. How many people, including myself, have sat on the side of the bed and cried, begging to God to make this stop."

“But unless it’s really personal. Unless it pertains to someone in healthcare, big pharma, drug companies, insurance companies, they don’t understand. Members have to go through multiple doctors to find the right one, something traveling great distances. Especially people in the rural area, drive hours for an appointment. But we’re in it for the long haul, and we all deserve the very best care.”

“In order to get a transplant, you have to be sick enough. And I think that’s such a bad way to think about things: you have to progress to a point where all the options are exhausted except transplant. People don’t realize the effects of the fatigue, itching, and joint pains. Marriages, family members, and friendships are lost. This is the way our lives are. This is the way it affects every aspect of our lives. We cancel social events because of the fatigue. We can’t go out in public because of the itching and scratching, which leaves marks on our arms and legs. We can’t remember the last time we slept well. But we’re not PBC. We’re so much more than the disease.”

## **Cathy Mumford**

“In dealing with clinical trials, it was a life-changing moment for me. It rocked me in ways that I thought nothing could. I realized I didn’t know a lot of things that I probably should know about cirrhosis, stage 4 liver disease, and disease progression, even though I was involved with PBCers for years by then. I had a hole in my knowledge base.”

“Debilitating fatigue and severe pruritus are the main symptoms I have. It changed my life considerably. If you have pruritus, you can’t sleep because of the itching. And the fatigue exacerbates it. There’s a story about living with really severe fatigue. It’s called the spoon theory. It’s a testament to what we deal with everyday. Because everyday I don’t know if I am going to have the energy to do anything. Can I take a shower, or go grocery shopping, or pursue my passions? Having cirrhosis is also unfortunately very stigmatizing. One time, I was in the emergency room, and the charge nurse stood at the door and told the nurse that was taking care of me, ‘Don’t waste resources on her, she’s got cirrhosis.’ The implication was very clear. Somehow I was unworthy of care because I had a disease that was destroying my liver.”

“Because of my interest in clinical trials and research, I am passionate as a patient advocate, patient, and support mechanism, to encourage everyone who can participate in a clinical trial, to do so. We cannot receive additional therapies to slow the progression or treat symptoms of the disease without participation at trials. I continue to live each day fully, and I am committed to patient advocacy, research, effective and safe treatments for PBC and symptoms, and someday, a cure.”

# Survey Results and Findings

**To supplement the input gathered at the meeting, GLI conducted a patient survey on the benefits and risks of potential treatments for PBC.** The survey sought insights into the PBC patient experience and highlighted unmet needs in PBC, especially in areas such as care pathways, treatments, and clinical trial access.

GLI utilized a variety of outreach mechanisms to reach a broad cross-section of the community in a wide array of situations, demographics, socioeconomic circumstances, capacities, and geographic locations. The survey collected anonymous information about the priorities and preferences of patients as **they address PBC by including questions about diagnosis, symptoms, liver biopsies, clinical trial access, and available treatment options.**

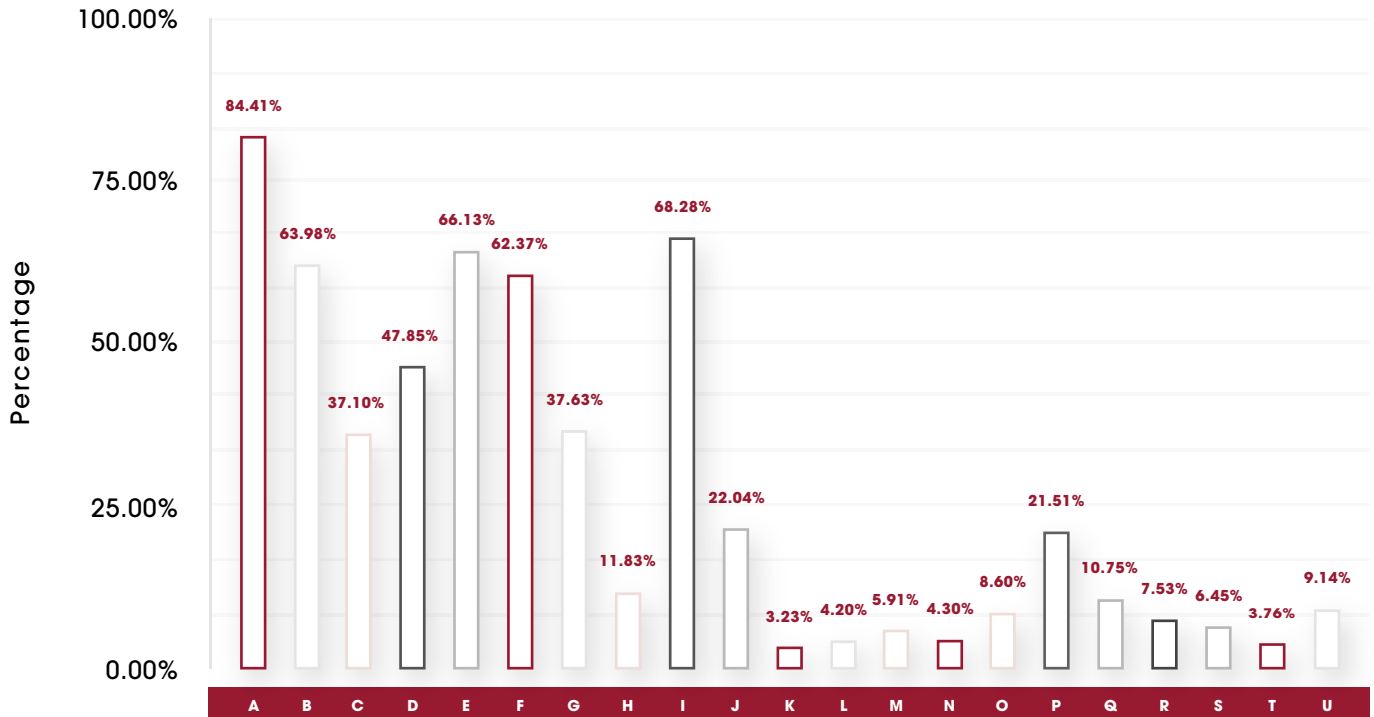
**Patients also shared their experience with clinical trials.** According to survey results, the largest barrier to participation in clinical trials was distance to research centers, followed by concerns about accommodation, meals, and transportation costs. Several factors could address this issue, including access to virtual care and trials, expanded understanding of PBC, access to new drugs, and monetary compensation for accommodation during the trial.

**Survey results provide insight into patients' perspectives on their most significant symptoms, the impact of PBC on quality of life, and treatment options.** Comments received reinforced the experiences and perspectives shared during the virtual meeting. The following information highlights these comments, with a focus on the experiences or perspectives that were not raised or addressed in detail at the meeting.

## Selected Survey Results Disease State and Symptom Questions

1. With regards to your PBC, to the best of your knowledge, do you currently have or have you previously had any of the following symptoms? Select all that apply.

### Previous and Current Symptoms in PBC Patients



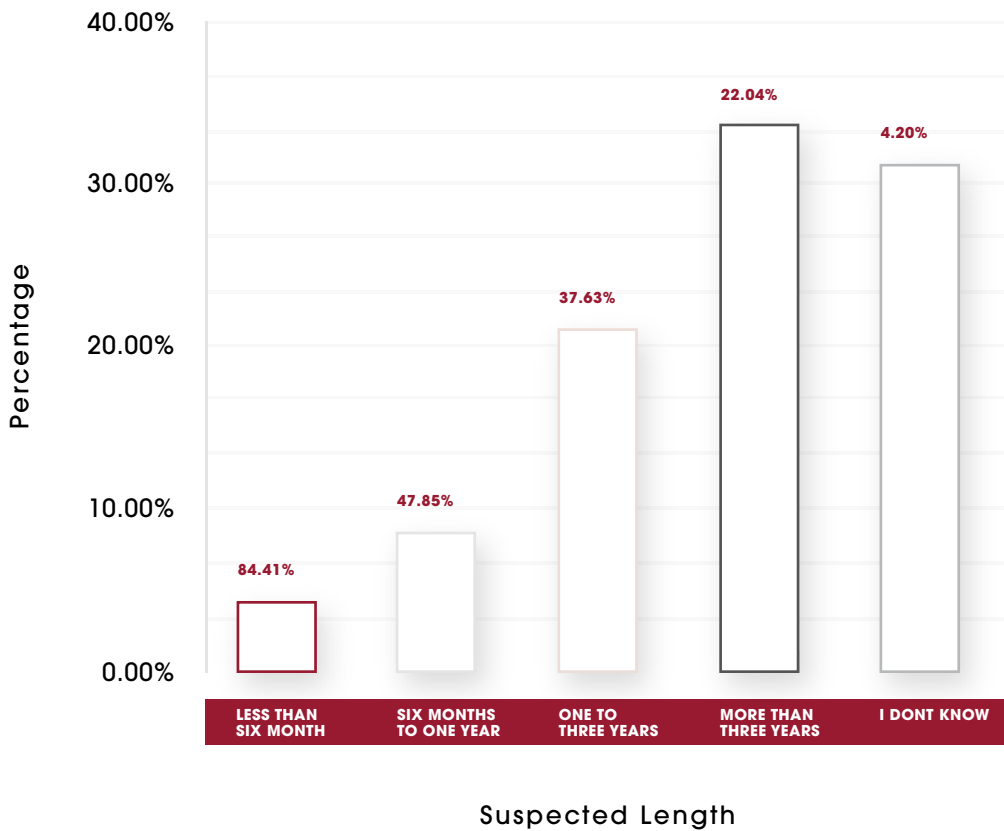
### Symptoms

- |          |  |          |   |
|----------|--|----------|---|
| <b>A</b> | Fatigue  | <b>M</b> | Yellowing of the skin and eyes (Jaundice)                                     |
| <b>B</b> | Itchy skin (Pruritus)  | <b>N</b> | Darkening of the skin that isn't related to sun exposure (Hyper Pigmentation) |
| <b>C</b> | Nausea   | <b>O</b> | Weak and brittle bones (Osteoporosis)   |
| <b>D</b> | Insomnia   | <b>P</b> | High Cholesterol  |
| <b>E</b> | Dry eyes and mouth   | <b>Q</b> | Diarrhea, which may include greasy stools (Steatorrhea)                       |
| <b>F</b> | Pain in the upper right abdomen                                | <b>R</b> | Underactive thyroid (Hypothyroidism)  |
| <b>G</b> | Pain in the right shoulder or upper back                       | <b>S</b> | Appetite loss   |
| <b>H</b> | Swelling of the spleen (Splenomegaly)                          | <b>T</b> | Weight loss   |
| <b>I</b> | Bone, muscle, or joint (Musculoskeletal) pain                  | <b>U</b> | Other (free response)   |
| <b>J</b> | Swollen feet and ankles (Edema)                                |          |   |
| <b>K</b> | Buildup of fluid in the abdomen due to liver failure (Ascites) |          |   |
| <b>L</b> | Fatty deposits (Xanthomas) on the skin around the eyes         |          |   |



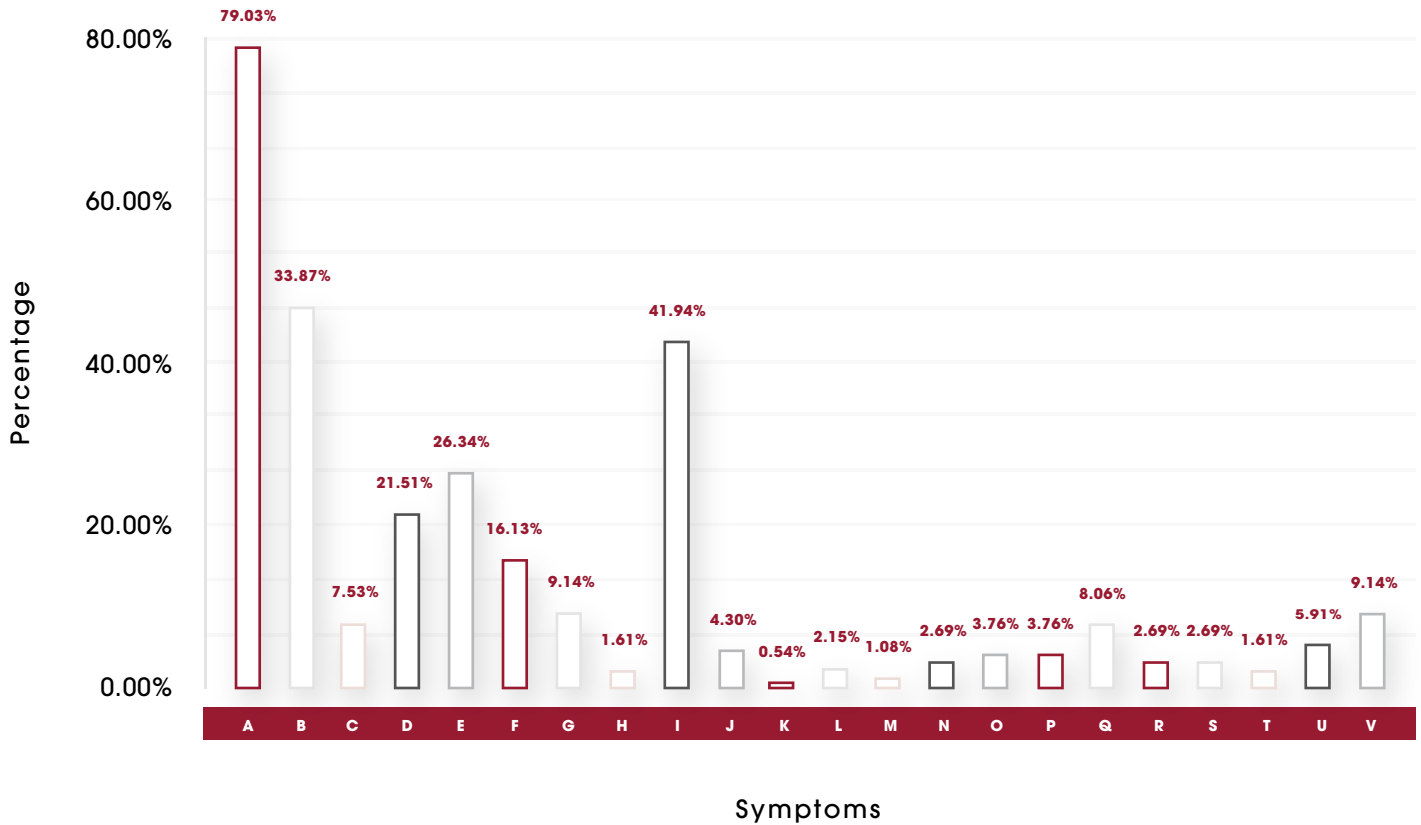
2. How long do you suspect you had PBC before you were diagnosed?

### Suspected length of PBC before diagnosis



3. Of the following symptoms of PBC, which have the most significant burden on your daily life? **Please select the top 3.**

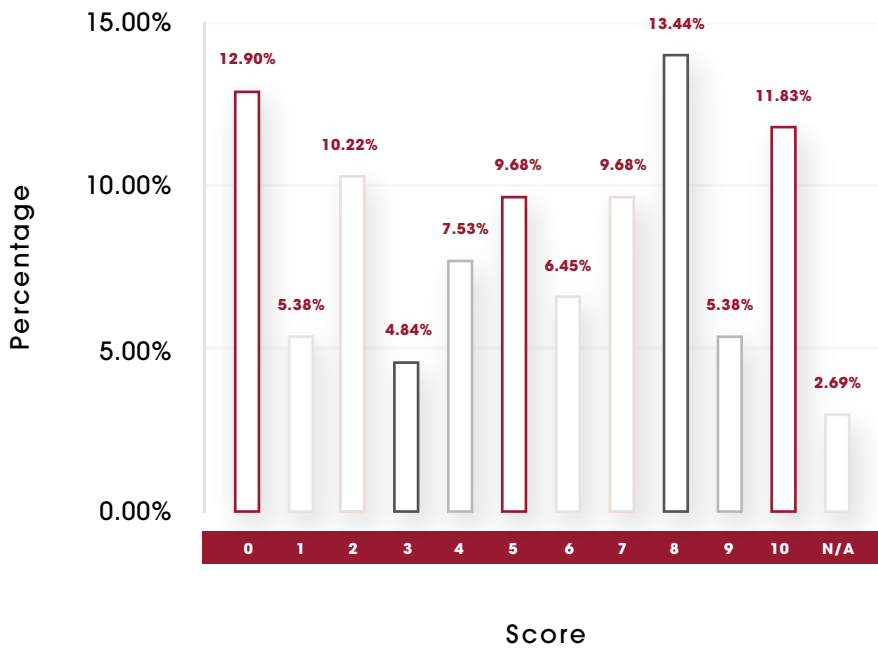
### PBC Symptoms with Significant Burdens



- |          |  |          |  |
|----------|--|----------|--|
| <b>A</b> | Fatigue  | <b>L</b> | Fatty deposits (Xanthomas) on the skin around the eyes, eyelids, or in the creases of the palms, soles, elbows, or knees |
| <b>B</b> | Itchy skin (Pruritus)  | <b>M</b> | Yellowing of the skin and eyes (Jaundice)  |
| <b>C</b> | Nausea   | <b>N</b> | Darkening of the skin that isn't related to sun exposure (Hyper Pigmentation)  |
| <b>D</b> | Insomnia   | <b>O</b> | Weak and brittle bones (Osteoporosis)  |
| <b>E</b> | Dry eyes and mouth   | <b>P</b> | High Cholesterol   |
| <b>F</b> | Pain in the upper right abdomen                                | <b>Q</b> | Diarrhea, which may include greasy stools (Steatorrhea)  |
| <b>G</b> | Pain in the right shoulder or upper back                       | <b>R</b> | Underactive thyroid (Hypothyroidism)   |
| <b>H</b> | Swelling of the spleen (Splenomegaly)                          | <b>S</b> | Appetite loss  |
| <b>I</b> | Bone, muscle, or joint (Musculoskeletal) pain                  | <b>T</b> | Weight loss  |
| <b>J</b> | Swollen feet and ankles (Edema)                                | <b>U</b> | Other (free response)  |
| <b>K</b> | Buildup of fluid in the abdomen due to liver failure (Ascites) |          |  |

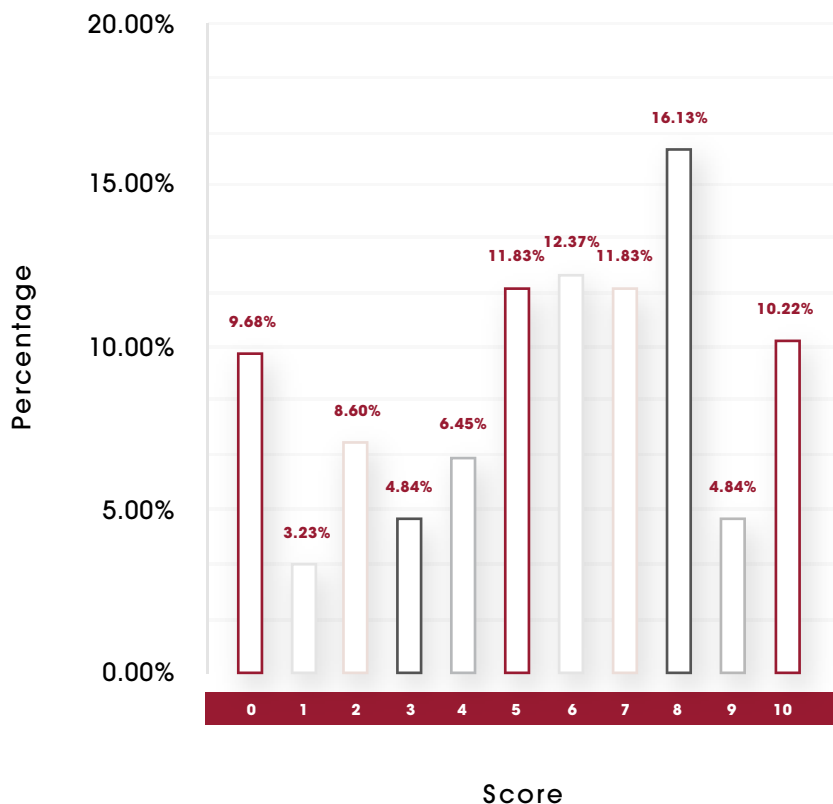
4. Please score 0-10 (10 being the worst interference) based on your feelings on this statement:  
*"The symptoms of PBC interfere with my work."*

### Scoring of Work Interference from PBC Symptoms



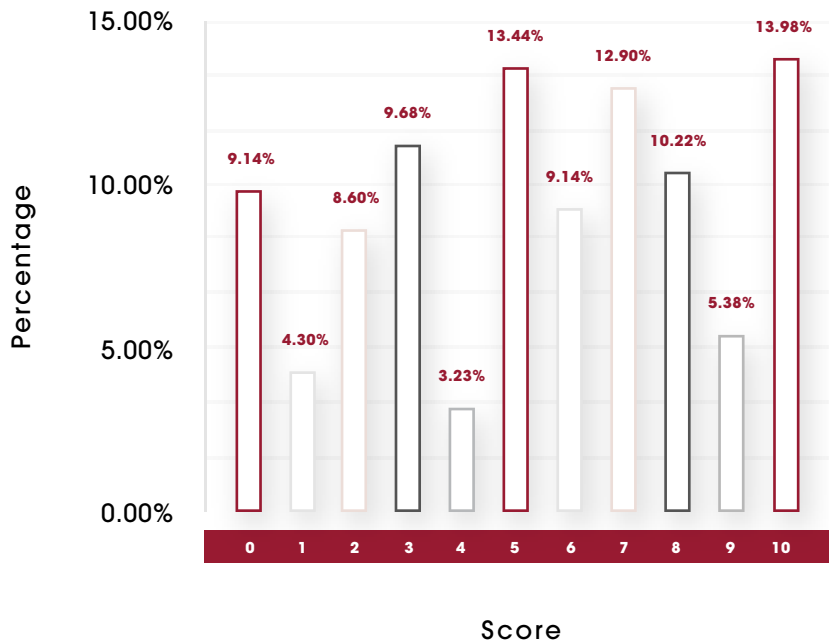
5. Please score 0-10 (10 being the worst interference) based on your feelings on this statement:  
*"The symptoms of PBC interfere with my daily activities."*

### 5. Scoring of Daily Activity Interference from PBC Symptoms



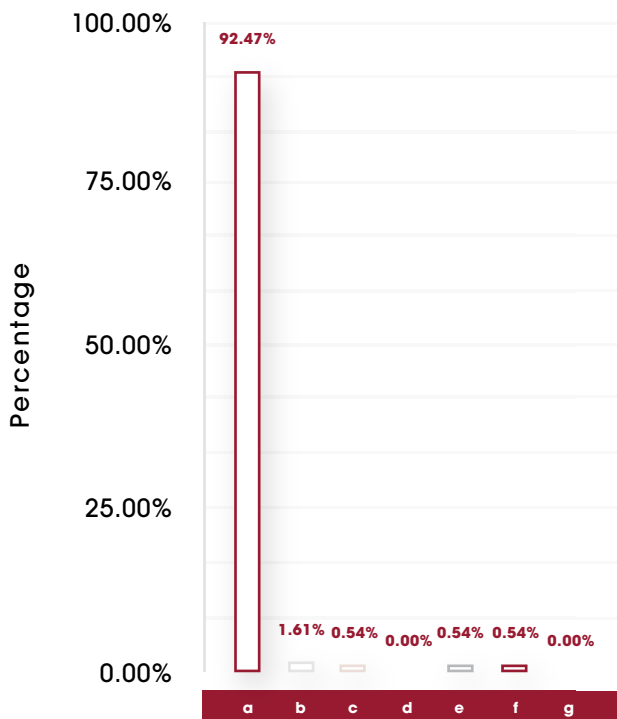
6. Please score 0-10 (10 being the worst interference) based on your feelings on this statement: "The symptoms of PBC interfere with my sleep."

### Scoring of Sleep Interference from PBC Symptoms



7. Have you been prescribed and/or do you use any of the following options as a treatment for PBC or it's symptoms?

### Usage of Treatment for PBC or It's Symptoms

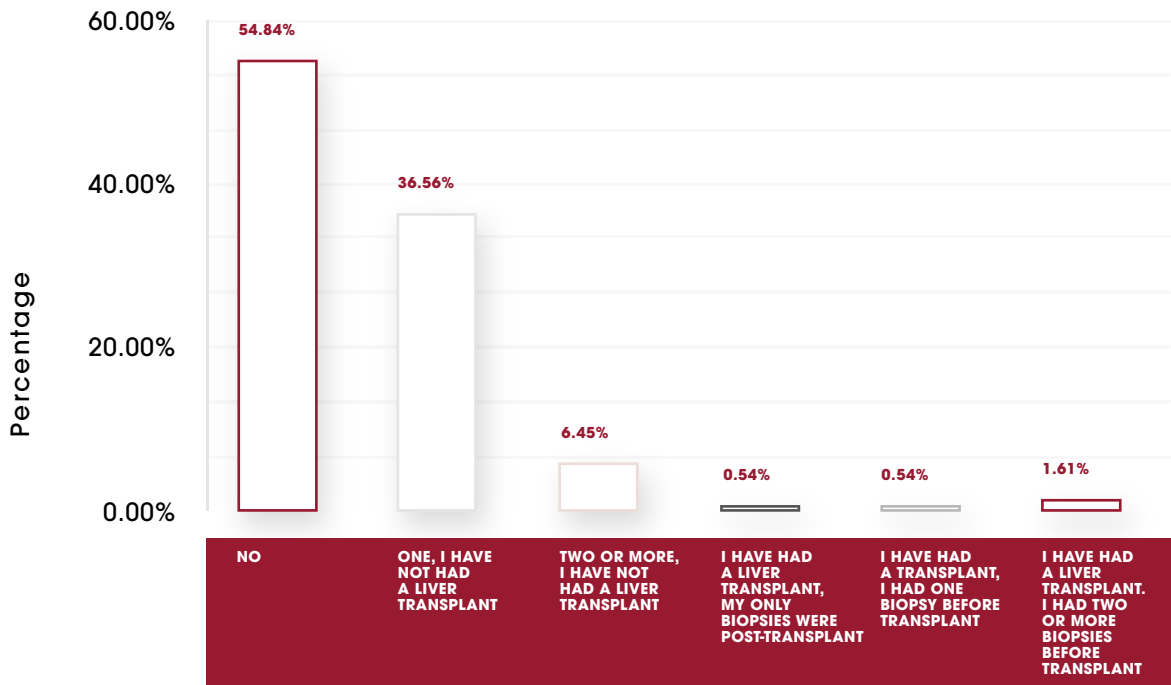


- A** Ursodeoxycholic acid
- B** Obeticholic acid (e.g. Ocaliva)
- C** Bezafibrate (e.g. Fenolip, Bezalip, Globez, Abeita)
- D** Fenofibrate (Antara, Fenoglidle, Lipofen, Lofibra, Tricor, Triglide)
- E** Colestyramine (e.g. Prevalite, Questran, Novo-Cholamine)
- F** Natural remedies (e.g. dandelion tea, turmeric, milk thistle)
- G** Other [free response]

Treatments

8. Have you ever had a liver biopsy? Select all that apply.

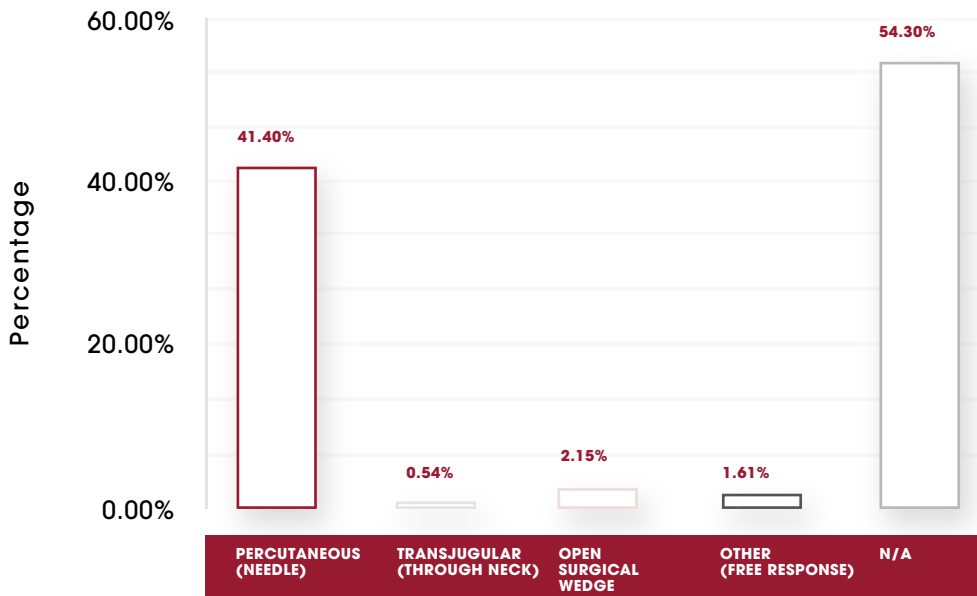
### Liver Biopsy Responses



### Responses

9. If you have had a liver biopsy, what type of liver biopsy was it?

### Types of Liver Biopsy



### Types

10. If you have had a liver biopsy, when was your most recent liver biopsy?

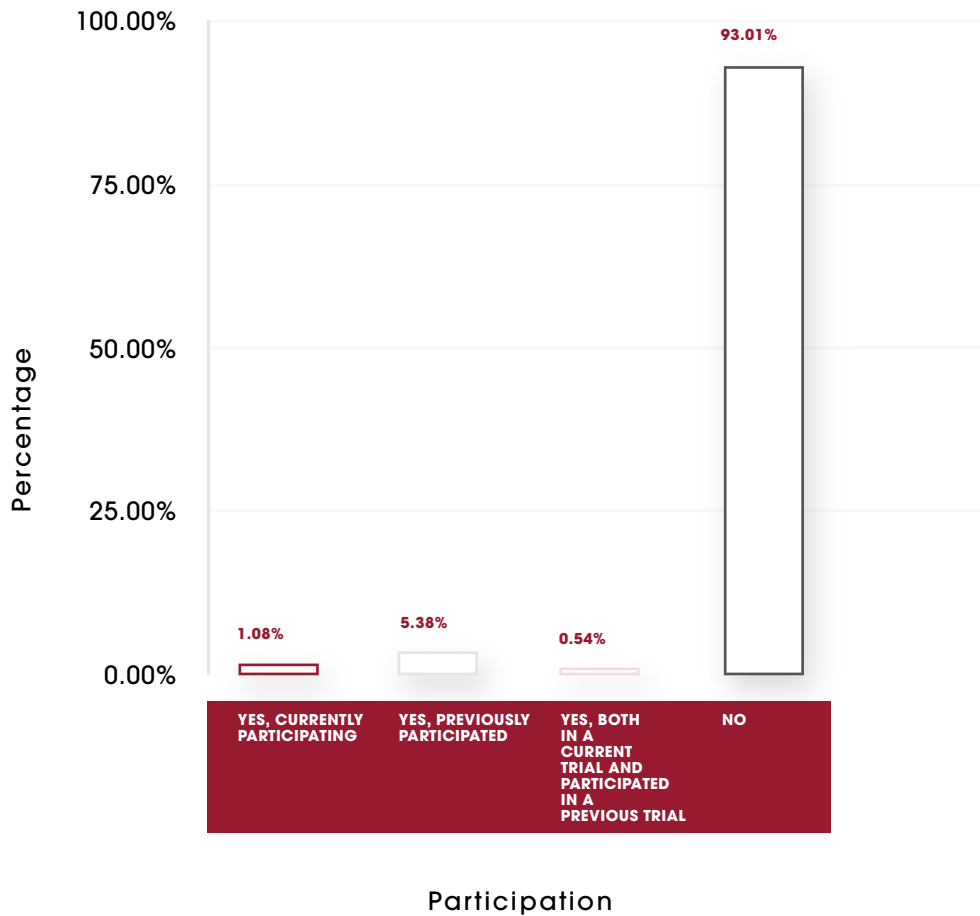
### Time of Recent Liver Biopsy

Time

### Treatment Options

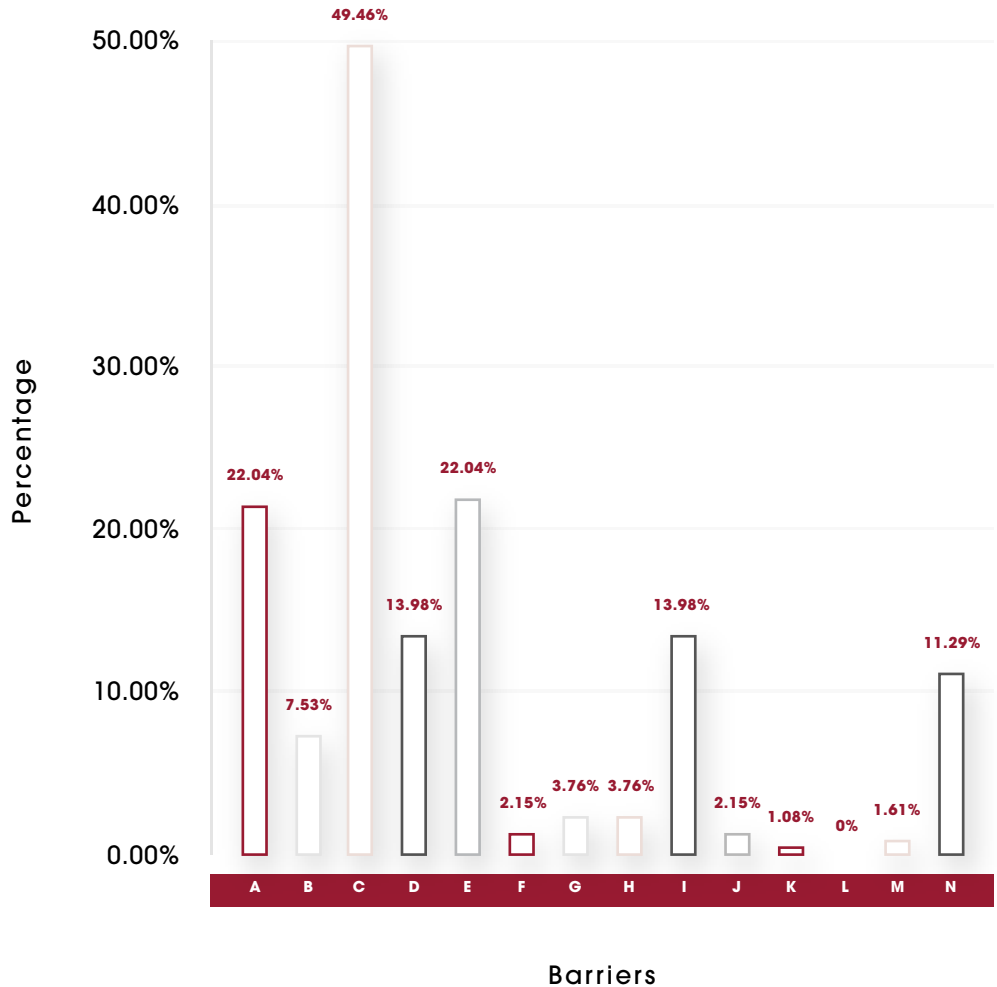
1. Have you participated or are you currently participating in a clinical drug trial?

### Participation in Clinical Drug Trials



2. Are there any barriers that might prevent you from participating in a clinical trial?  
 If yes, what are they? **Select all that apply.**

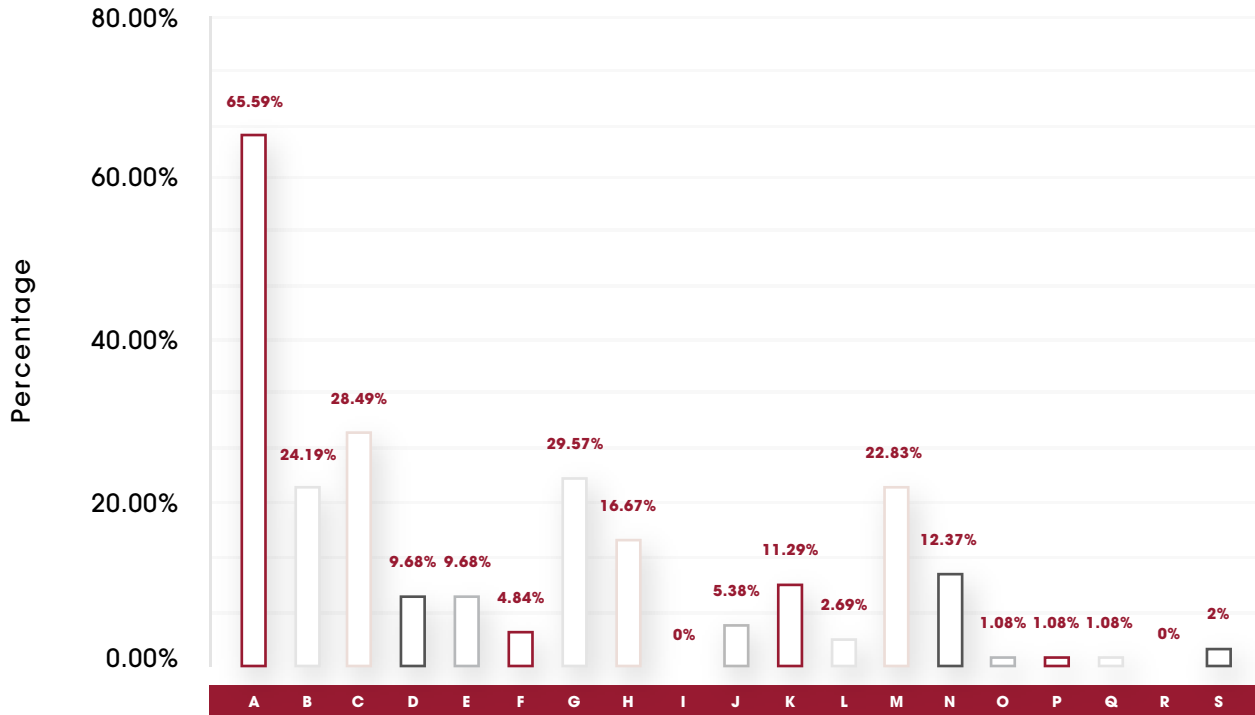
### Barriers to Participating in Clinical Trials



- A** Taking time off work or school
- B** Child/adult care
- C** Distance to research centers
- D** Concerns around upfront care costs
- E** Concerns about accommodation, meals, and transportation costs
- F** Poor or no WiFi connection
- G** Mistrust of medical system
- H** Bad prior experience with medical system
- I** Biopsy
- J** Fasting
- K** Bloodwork
- L** Filling out surveys
- M** Pregnancy or planned pregnancy
- N** Other [free response]

3. What are some factors or support services that may make you more likely to participate in a clinical trial? **Select all that apply.**

### Factors that Positively Influence Clinical Trial Participation

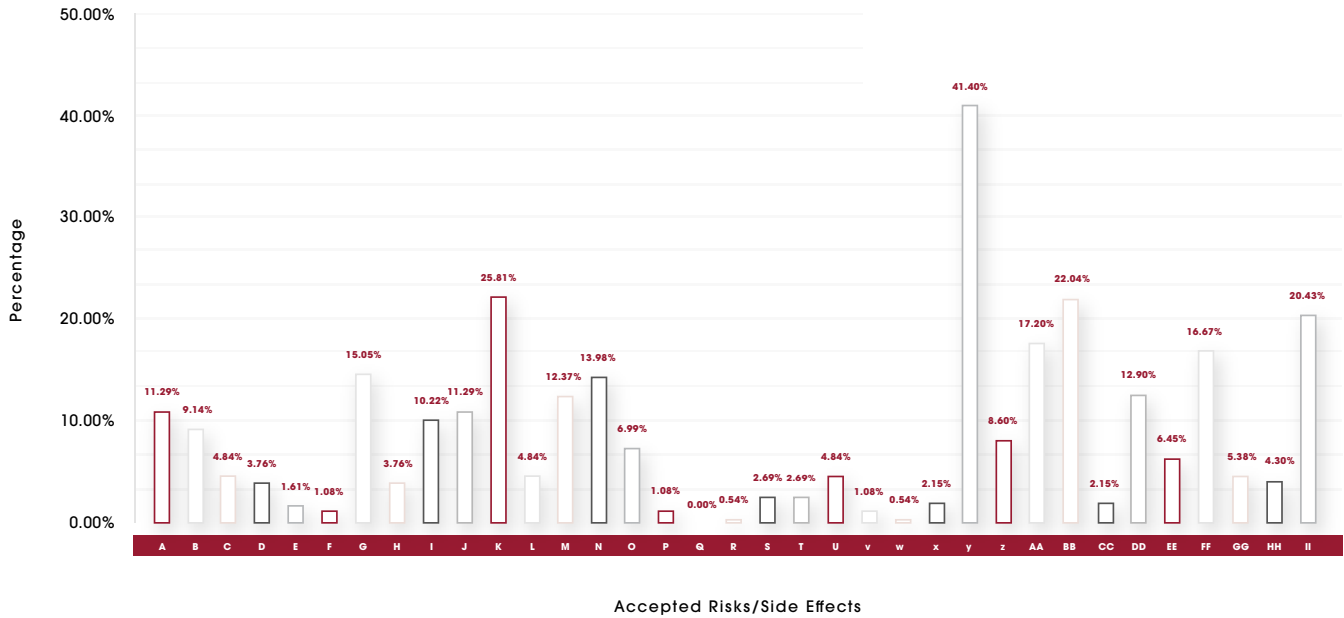


#### Factors

- A** Decentralized trials
- B** 24/7 telehealth support
- C** Online chat support
- D** Study call center (on-call staff available to help)
- E** Support groups
- F** Access to patient navigator
- G** Contribution to what we understand about PBC
- H** Access to new drugs
- I** New diagnostic testing
- J** Monetary compensation for time, travel costs, and/or child/adult care
- K** Periodic updates about the progress of the study
- L** Clinical trial advisory sessions (with sponsors and health care professionals) to design the clinical study
- M** Receiving a summary of the study results once the study is completed
- N** Gaining greater awareness about PBC
- O** Talking to health care professionals or clinical trial administrators about how they designed the clinical trials
- P** Providing input on the outcomes (i.e., biochemical baseline measurements, median overall survival, duration of study) measured in the clinical trial
- Q** Surveys that ask about your preferences for treatments
- R** Translation services (services translated into my language)
- S** Other [free response]

4. If the benefits included treatment or relief from your PBC symptoms, which of the following risks or side effects would you accept?

### Accepted Risks/Side Effects for PBC Treatment



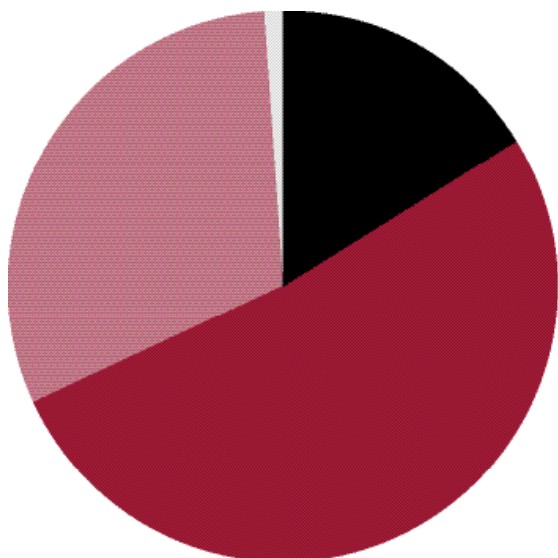
- |          |                               |           |  |
|----------|-------------------------------|-----------|--|
| <b>A</b> | Dizziness                     | <b>S</b>  | Eye damage   |
| <b>B</b> | Itching                       | <b>T</b>  | Tremors  |
| <b>C</b> | Depression                    | <b>U</b>  | Twitching  |
| <b>D</b> | Anxiety                       | <b>V</b>  | Hallucinations   |
| <b>E</b> | Mania                         | <b>W</b>  | Agitation/Irritability                                   |
| <b>F</b> | Suicidal thoughts or ideation | <b>X</b>  | Overactive reflexes                                      |
| <b>G</b> | Nausea                        | <b>Y</b>  | Loss of appetite   |
| <b>H</b> | Vomiting                      | <b>Z</b>  | Increase of appetite                                     |
| <b>I</b> | Diarrhea                      | <b>AA</b> | Sore throat  |
| <b>J</b> | Drowsiness                    | <b>BB</b> | Runny nose   |
| <b>K</b> | Dry mouth                     | <b>CC</b> | Nightmares   |
| <b>L</b> | Insomnia                      | <b>DD</b> | Loss in sexual ability, desire, drive,<br>or performance |
| <b>M</b> | Constipation                  | <b>EE</b> | Joint pain, stiffness, or swelling                       |
| <b>N</b> | Headache                      | <b>FF</b> | Dry skin   |
| <b>O</b> | Rash                          | <b>GG</b> | Restlessness   |
| <b>P</b> | Kidney damage                 | <b>HH</b> | Hair loss  |
| <b>Q</b> | Kidney damage                 | <b>II</b> | Hair growth  |
| <b>R</b> | Pancreatitis                  |           |  |



## Demographic Questions

1. What is your age?

### Age

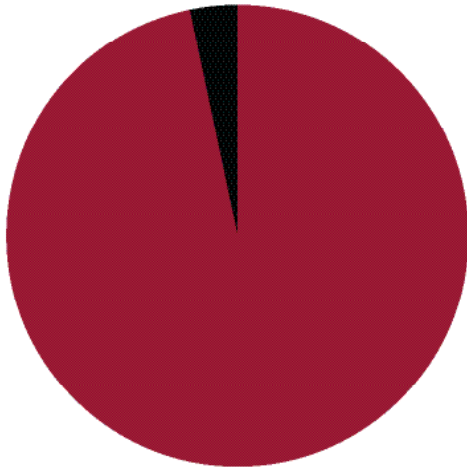


- 31-45
- 46-60
- 61-75
- 79-90

2. What is your biological sex?

### Biological Sex

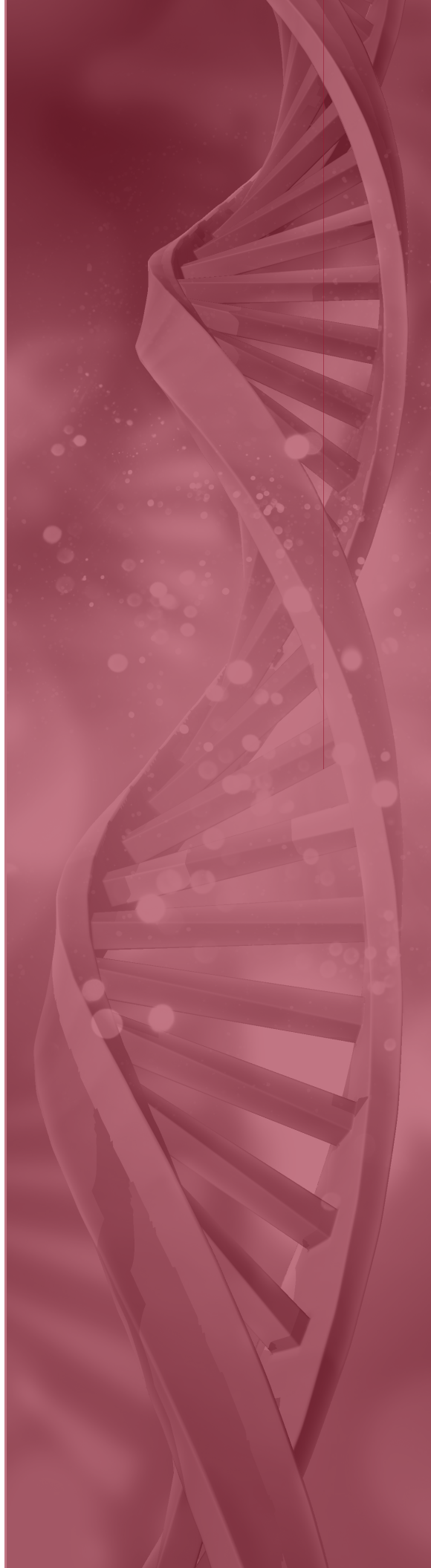
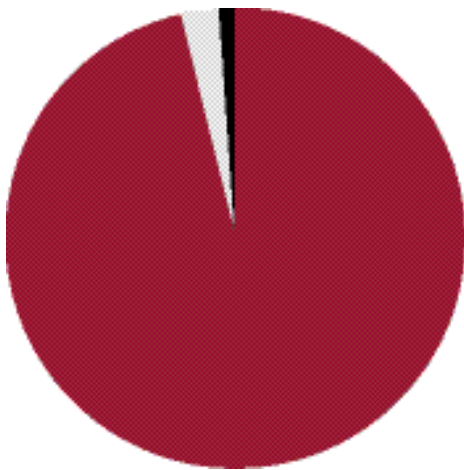
- Female
- Male



3. What is your gender identity?

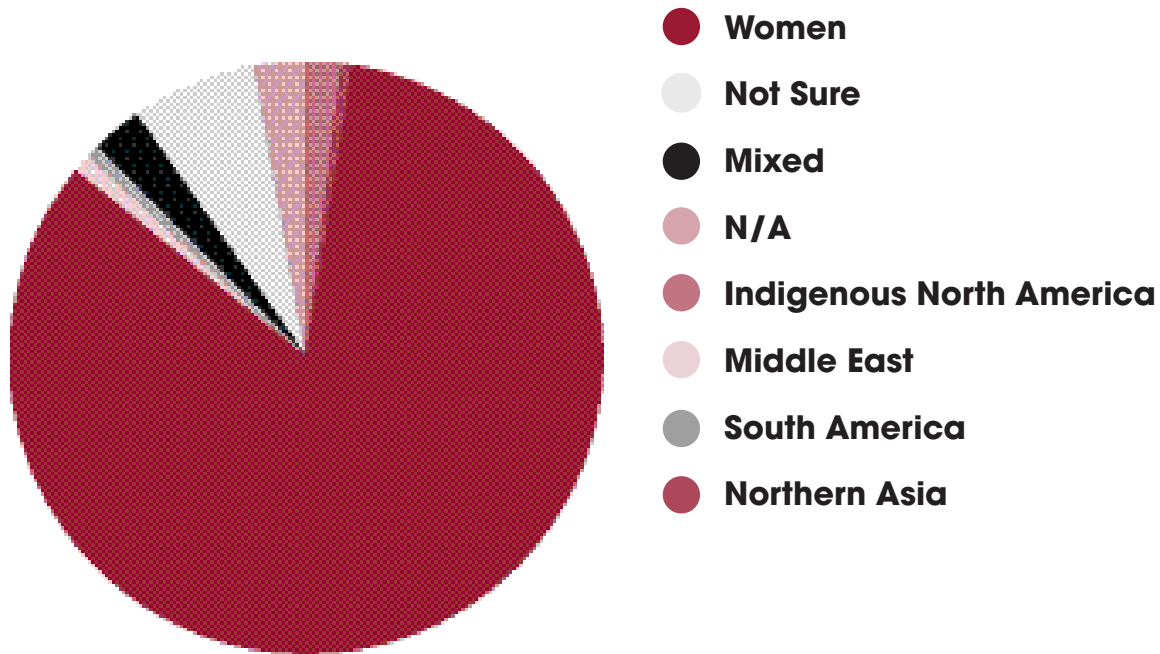
### Gender Identity

- Women
- Man
- N/A



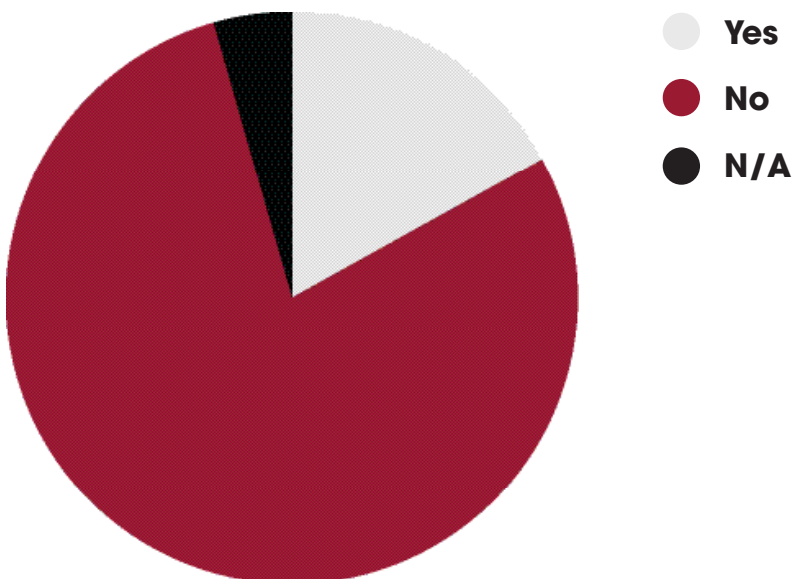
4. From where would you place your genetic heritage? (We are looking to explore genetic aspects to Urso response, symptom burden, etc, so we are looking at racial genetic aspects, as opposed to cultural or ethnic history)

### Genetic Heritage

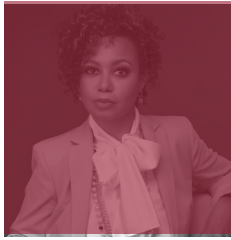


5. Are you interested in speaking to the U.S. FDA, pharmaceutical and biotechnological representatives, academics, clinicians, etc. on behalf of the PBC community, e.g. during the Global Liver Institute’s Externally-Led Patient-Focused Drug Development Forum on February 4, 2022? The meeting will be virtual and speaking slots will be approximately five minutes. If yes, please provide a brief summary of your PBC journey and your email address. This question will not be cross-referenced with any other question so your data will remain anonymous.

### Interest in PBC EI-PFDD Forum Participation



# Bios



**Moderators:**

**Donna R. Cryer, JD**  
**President & CEO,**  
**Global Liver Institute**

Donna R. Cryer, JD is Founder, President and Chief Executive Officer of Global Liver Institute, the only patient-driven liver health nonprofit operating across the US, EU, and UK. GLI convenes the NASH, Liver Cancer and Pediatric and Rare Liver Disease Councils, as well as the Liver Action Network, collectively more than 200 organizations.

**Mrs. Cryer has channeled her personal experience as a patient with inflammatory bowel disease and a 28-year liver transplant recipient into professional advocacy across a career in law, policy, consulting, public relations, clinical trial recruitment, and nonprofit management.** She is the recipient of the 2021 Global Genes RARE Champions of Hope Founder's Award and the 2021 AASLD Distinguished Advocacy Service Award.

**At GLI, Mrs. Cryer has raised more than \$10 million for liver health initiatives.** Among her many accomplishments with GLI, she developed a program featured by the White House on Solving Organ Shortage/Transplantation. She has launched numerous other successful programs at GLI, including the Cure Campaign, Advanced Advocacy Academy (A3), Liver Matters Blog, Liver Matters Health Policy Memo, the NASH Council, the Liver Cancers Council and the Pediatric and Rare Liver Diseases Council.

She is a frequent speaker on the topic of patient-centeredness and patient engagement in healthcare transformation and created a unique model for advocacy that mobilizes patients, influences policy, and coalesces clinicians to improve patient outcomes. In May 2021, she testified before the U.S. House Committee on Oversight and Reform, Subcommittee on Economic and Consumer Policy, in a pivotal hearing on reforming the broken organ procurement system. Her testimony highlighted the racial disparities in organ transplantation. Thanks to consistent, fact-based advocacy from GLI, other allied groups, the media, and Congress, meaningful reforms to improve the system are finalized and forthcoming. Her advocacy for better representation of people of color in the organ procurement system includes urging the U.S. Office of Management and Budget to implement three concrete steps she identified to facilitate more transplants for people of color and an elevated performance for the entire system, benefiting all patients.

Mrs. Cryer received an undergraduate degree from Harvard and a Juris Doctorate from the Georgetown University Law Center.



**Moderator:**

**Robert Mitchell-Thain,  
CEO, PBC Foundation;  
Chairman, Pediatric and Rare Liver Diseases Council,  
Global Liver Institute**

Robert Mitchell-Thain is considered as one of the most outstanding and inspirational leaders in the rare disease space, who continues to pave the way for patients and empower them to take charge of their own health and care management. In the healthcare industry, Robert provides a unique perspective – the patient perspective, with the addition of the caregiver’s viewpoint. **As a liver patient and a caregiver himself, Robert fights to raise awareness on rare liver diseases like primary biliary cholangitis (PBC) and tackle challenges that many PBC and rare liver disease patients and caregivers face.** Without his fierce efforts in advocating for the rare community, many of the innovations that he has spearheaded would cease to exist.

**He designed and presented a series of self-management modules, focusing on emotional, psychological and physical self-care of those affected by incurable conditions.** His models have been used by liver patients, lipoedema patients, epilepsy patients, ME and CFS patients and caregivers. These self-care modules have supported patients in Australia, Japan, Israel, UK, Canada and US, not to mention many countries in Europe. During Covid, he took to facebook live so as to reach patients around the world with rare autoimmune diseases, such as PBC, and presented for over 200 consecutive days live running quizzes, games, live music sessions and self-care and patient education seminars, bringing together the PBC population from six continents.

After 19 years in the liver community, he has proven himself as a Champion of Hope and stands at the top with the rest of the clinicians, industry leaders, and patient advocates who vigorously and continuously work hard to provide patients and caregivers with resources to manage their health better. Robert was one of the earliest patient advocates to be involved in co-authoring journal pieces, abstracts and clinical care guidelines. He has also led the field in writing lay versions of guidelines, ensuring more patients had access to the information they needed in order to empower themselves in their patient journey. Removal of the “cirrhosis” stigma, and its implications of alcohol abuse, particularly for newly-diagnosed patients. Robert led the international campaign to change the name for PBC (primary biliary cirrhosis to primary biliary cholangitis), and presented to an EASL monothematic conference in Milan highlighting the challenges faced by PBC patients beyond living with a progressive, incurable condition.

Throughout the years, Robert Mitchell-Thain has made a large contribution in increasing advocacy for patients, spreading awareness of rare liver diseases, and empowering every group in the care team. The recent UK-wide audit of PBC care undertaken by the NHS cited Robert’s work highlighting the unmet need in patient experiences in PBC care.

# Panelists:

## Levinia Ashanti

In 2018, Levinia was diagnosed with PBC. Currently, she lives in England, where she battles several debilitating symptoms of PBC with the support of her family and friends. Thanks to all the support she received, she is able to live her life as normally and healthily as possible.

## Donna Boll

Donna was diagnosed with PBC at the age of 35 after 5 years of investigation and 9 liver biopsies. She is now 71 years old and is 17 years post-transplant. She helps facilitate support groups for around 3000 PBC patients.

## Richard Cook

Richard was diagnosed with PBC in 2019, shortly after a bad fall and a subsequent diagnosis of osteoporosis. After being treated with Ursodeoxycholic Acid (UDCA), he continues to experience symptoms. He lives in his childhood hometown in a rural area of northeastern Michigan and remains active and positive despite his symptoms of PBC.

## Mo Christie

In 2017, Mo was diagnosed with PBC and immediately began treatment. Unfortunately, she was not responsive to UDCA. Currently, she lives in Scotland with her husband Mark and their daughter Eve. To continue spreading awareness of PBC and advocating for patients, she volunteers at the PBC Foundation in Scotland.

## Danielle Cleary

Danielle Cleary, a patient born in El Salvador who lives in Boston, MA, was diagnosed with PBC with AIH overlap in 2020.

## Doreen Donaldson

Doreen is a patient who was diagnosed with PBC in 1988. She continues to experience symptoms associated with PBC since her diagnosis. She decided to work as a patient advocate to create more awareness on PBC in Australia due to inadequate treatment.

## Doreen Donaldson

Doreen is a patient who was diagnosed with PBC in 1988. She continues to experience symptoms associated with PBC since her diagnosis. She decided to work as a patient advocate to create more awareness on PBC in Australia due to inadequate treatment.

## **Angela Eddy**

Angela was diagnosed with PBC 12 years ago and received a liver transplant 2 years after the initial diagnosis. She has been involved in several clinical trials.

## **Cathy Mumford**

Cathy currently resides in Hawaii. She had abnormal liver biochemistry for years before diagnosis with PBC in 2006 with early stage I PBC. She has participated in 4 clinical trials since and is actively involved in the PBCers organization.

## **Carol Roberts**

Carol was diagnosed with PBC early in 1999. Her symptoms were treated with UDCA. Her mission is to raise awareness about PBC and actively support patients with the disease as the conference organizer and president of PBCers. She characterizes herself as a “big-time advocate” for PBC patients.

## **Leslie Stratta**

Leslie is a transformation coach and an HR executive, living in Houston, Texas. In the summer of 2017, she was diagnosed with PBC, and has since been an active patient advocate through coaching, support groups, therapy strategies, and meditation.

## **Collette Thain**

Collette is a PBC patient in the UK and is the leader of over 15,000 other PBC patients in support groups all over the world. 25 years ago, she was diagnosed with PBC at the age of 37.

## **Bob Tyler**

A patient who was diagnosed with PBC and AIH concurrently 9 years ago. Bob is from Cleveland, Ohio, and currently struggles with the pain associated with PBC.

## **Deborah Sobel**

Deborah has been living with an autoimmune disease that targets her liver for more than 30 years. Her sister, who was diagnosed with PBC around the time of Deborah’s original diagnosis, was also a passionate patient advocate but passed away in 2016.

## **Gail Wright**

As a patient with PBC herself, Gail recognizes the lack of resources for rare diseases in Canada. This led to her becoming the president of the Canadian PBC Society. As part of her research, she analyzes PBC patterns in Cowichan tribes, the biggest First Nations community in Vancouver, British Columbia.

# Conclusion

**Primary biliary cholangitis, or PBC is a chronic, autoimmune cholestatic liver disease that affects the bile ducts.** Overtime, PBC can worsen and potentially lead to cholestasis and end-stage liver disease if it is not treated adequately. Although relatively rare, PBC is the most common liver disease associated with chronic cholestasis in adults with a prevalence of about 39.2 per 100,000 inhabitants. In effort to spread awareness on PBC, GLI conducted a GLI-led EL-PFDD meeting on PBC, offering an opportunity for regulators (such as the FDA) and drug developers to hear directly from patients and caregivers.

Overall, the PBC EL-PFDD successfully informed and drove forward the next generation of clinical trials and treatment approvals by encompassing the unmet needs of PBC patients, their daily lives, available therapies for symptom management, and improvements in future treatments for PBC.



# Appendix

## Meeting Agenda

10:00 am - 4:30 pm EST Virtual (Zoom)

### TOPIC

### SPEAKER

Opening Remarks

**Donna Cryer, JD**

President & CEO  
Global Liver Institute

PFDD Overview and Objectives

**Director Joseph Toerner, MD**

Division of Hepatology and  
Nutrition  
U.S. Food and Drug  
Administration

Clinical Features of PBC

**Dr. Marco Carbone, MD, PhD**

Assistant Professor of  
Gastroenterology  
University of Milan-Bicocca

# Appendix

## TOPIC

## SPEAKER

How Does PBC Affect My Life?

*Panelists - Patient  
Testimonial Videos*

**Overview and Relevant Results  
of PFDD Survey,  
and Polling Questions**

*Robert Mitchell-Thain*  
Pediatric and Rare Liver Diseases  
Chairman of GLI's Pediatric and  
Rare Liver Diseases Council

**Open Forum Q&A –  
Zoom Discussion Starters**

*Bob Tyler*  
*Levinia Ashanti*  
*Richard Cook*  
*Leslie Stratta*  
*Carol Roberts*  
*Mo Christie*

Break

Break

Current Therapeutic Approaches

**Prof. Dave Jones, OBE**  
Director of Newcastle Centre for  
Rare Disease  
Professor of Immunology  
Newcastle University

How Does Current Therapeutic  
Landscape Affect My Life?

**Panelists - Patient Testimonial  
Videos**

**Overview and Relevant Results  
of PFDD Survey, and Polling  
Questions**

*Robert Mitchell-Thain*

**TOPIC****SPEAKER****Open Forum Q&A –  
Zoom Discussion Starters**

*Doreen Donaldson*

*Gail Wright*

*Deborah Sobel*

*Danielle Cleary*

*Collette Thain*

Break

Break

The Future of Clinical Trials

**Cynthia Levy, MD**

Assistant Director for the Schiff  
Center for Liver Diseases  
University of Miami

How Can We Design an Ideal  
Clinical Trial?

**Panelists - Patient Testimonial  
Videos**

Overview and Relevant Results  
of PFDD Survey, and Polling  
Questions

*Robert Mitchell-Thain*

**Open Forum Q&A –  
Zoom Discussion Starters**

*Angela Eddy*

*Donna Boll*

*Cathy Mumford*

Closing Remarks

**Donna Cryer, JD**

President & CEO  
Global Liver Institute

# Panel Questions

## **Panel 1 Theme**

Impact of patient support groups on quality of life; Importance of being a part of a registry

*What affects quality of life most for patients?*

*What is the impact of stress on your PBC?*

## **Panel 2 Theme**

Impact of patient support groups and clinical trials

*How does patient advocate groups and clinical trials help?*

*How does one validate measure that looks at quality of life?*

## **Panel 3 Theme**

Barriers to accessibility to clinical trials

*What can we do as a PBC community to help address barriers to accessibility to clinical trials?*

*Should people partake in biopsies with a clinical trial?*

*What are the implications for studies, results, and participation following inconsistent and inequitable care?*

*How close are we to incorporating a synthetic control PBC disease progression trial?*

*What are the best outcomes for PBC patients going into the future?*

# Patient Survey on Benefits and Risks of Potential Treatments for Primary Biliary Cholangitis (PBC)

Overall, the PBC EL-PFDD successfully informed and drove forward the next generation of clinical trials and treatment approvals by encompassing the unmet needs of PBC patients, their daily lives, available therapies for symptom management, and improvements in future treatments for PBC.

## 1. With regards to your PBC, to the best of your knowledge, do you currently have or have you previously had any of the following symptoms? Select all that apply.

- Fatigue
- Itchy skin (pruritus)
- Nausea
- Insomnia
- Dry eyes and mouth
- Pain in the upper right abdomen
- Pain in the right shoulder or upper back
- Swelling of the spleen (splenomegaly)
- Bone, muscle, or joint (musculoskeletal) pain
- Swollen feet and ankles (edema)
- Buildup of fluid in the abdomen due to liver failure (ascites)
- Fatty deposits (xanthomas) on the skin around the eyes, eyelids, or in the creases of the palms, soles, elbows, or knees
- Yellowing of the skin and eyes (jaundice)
- Darkening of the skin that isn't related to sun exposure (hyper pigmentation)
- Weak and brittle bones (osteoporosis)
- High cholesterol
- Diarrhea, which may include greasy stools (steatorrhea)
- Underactive thyroid (hypothyroidism)
- Appetite loss
- Weight loss
- Other [free response]

## 2. How long do you suspect you had PBC before you were diagnosed?

- Less than six months
- Six months to one year
- One to three years
- More than three years
- I don't know

## 3. Of the following symptoms of PBC, which have the most significant burden on your daily life? Please select the top 3.

- Fatigue
- Itchy skin (pruritus)
- Nausea
- Insomnia
- Dry eyes and mouth
- Pain in the upper right abdomen
- Pain in the right shoulder or upper back
- Swelling of the spleen (splenomegaly)
- Bone, muscle, or joint (musculoskeletal) pain
- Swollen feet and ankles (edema)
- Buildup of fluid in the abdomen due to liver failure (ascites)
- Fatty deposits (xanthomas) on the skin around the eyes, eyelids, or in the creases of the palms, soles, elbows, or knees

- Yellowing of the skin and eyes (jaundice)
- Darkening of the skin that isn't related to sun exposure (hyper pigmentation)
- Weak and brittle bones (osteoporosis)
- High cholesterol
- Diarrhea, which may include greasy stools (steatorrhea)
- Underactive thyroid (hypothyroidism)
- Appetite loss
- Weight loss
- Abdominal pain
- Other [free response]

**4. Please score 0-10 (10 being worst interference) based on your feelings on this statement:**

**“The symptoms of PBC interfere with my work.”**

- [Scale 0-10]

**5. Please score 0-10 (10 being worst interference) based on your feelings on this statement:**

**“The symptoms of PBC interfere with my daily activities.”**

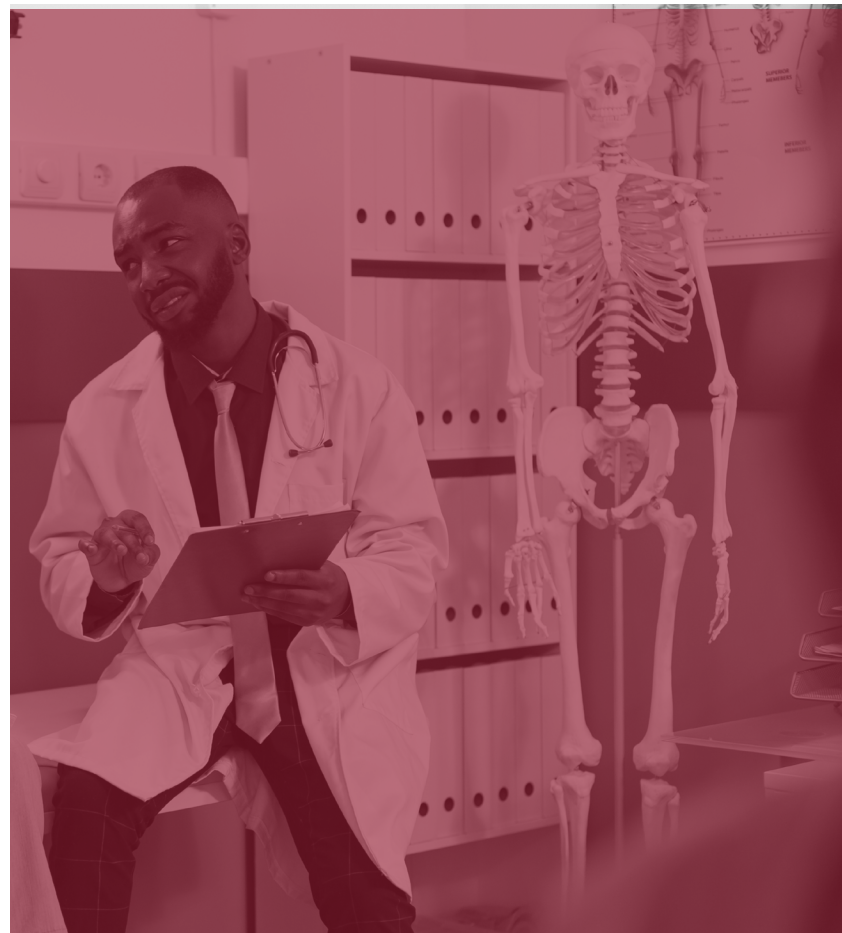
- [Scale 0-10]

**6. Please score 0-10 (10 being worst interference) based on your feelings on this statement: “The symptoms of PBC interfere with my sleep.”**

- [Scale 0-10]

**7. Have you been prescribed and/or do you use any of the following options as a treatment for PBC or its symptoms?**

- Ursodeoxycholic acid (e.g. UDCA, Ursodiol, Ursetor, Udikast, Actibile, Actigall, Biliver, Deursil, Egyurso, Udcasid, Udiliv, Udinorm, Udoxyl, Urso, Urso Forte, Ursocol, Ursoliv, Ursofalk, Ursosan, Ursoserinox, Udimarín, Ursonova, Stener)
- Obeticholic acid (e.g. Ocaliva)
- Bezafibrate (e.g. Fenolip, Bezalip, Globez, Abeita)
- Fenofibrate (Antara, Fenoglide, Lipofen, Lofibra, Tricor, Triglide)
- Colestyramine (e.g. Prevalite, Questran, Novo-Cholamine)
- Natural remedies (e.g. dandelion tea, turmeric, milk thistle)  
Other [free response]



**8. Have you ever had a liver biopsy?**

**Select all that apply.**

- No
- One, I have not had a liver transplant
- Two or more, I have not had a liver transplant
- I have had a liver transplant, my only biopsies were post-transplant
- I have had a transplant, I had one biopsy before transplant
- I have had a liver transplant. I had two or more biopsies before transplant.

**9. If you have had a liver biopsy, what type of liver biopsy was it?**

- Percutaneous (needle)
- Transjugular (through neck)
- Open surgical wedge
- Other [free response]

**10. If you have had a liver biopsy, when was your most recent liver biopsy?**

- Within the last six months
- Six months - One year
- One - Five years

**11. Have you participated or are you currently participating in a clinical drug trial?**

- Yes, currently participating
- Yes, previously participated
- Yes, both in a current trial and

participated in a previous trial

- No

**12. Are there any barriers that might prevent you from participating in a clinical trial? If yes, what are they? Select all that apply.**

- Taking time off work or school
- Child/adult care
- Distance to research centers
- Concerns around upfront care costs
- Concerns about accommodation, meals, and transportation costs
- Poor or no WiFi connection
- Mistrust of medical system
- Bad prior experience with medical system
- Biopsy
- Fasting
- Bloodwork
- Filling out surveys
- Pregnancy or planned pregnancy
- Other [free response]

**13. What are some factors or support services that may make you more likely to participate in a clinical trial? Select all that apply.**

- Decentralized trials (participate remotely, parts done at home, by mail, phone video, or otherwise - not requiring you to go to a research site or clinic)
- 24/7 telehealth support
- Online chat support
- Study call center (on-call staff available to help)
- Support groups
- Access to patient navigator
- Contribution to what we understand about PBC
- Access to new drugs
- New diagnostic testing
- Monetary compensation for time, travel costs, and/or child/adult care

- Periodic updates about the progress of the study
  - Clinical trial advisory sessions (with sponsors and health care professionals) to design the clinical study
  - Receiving a summary of the study results once the study is completed
  - Gaining greater awareness about PBC
  - Talking to health care professionals or clinical trial administrators about how they designed the clinical trials
  - Providing input on the outcomes (i.e., biochemical baseline measurements, median overall survival, duration of study) measured in the clinical trial
  - Surveys that ask about your preferences for treatments
  - Translation services (services translated into my language)
  - Other [free response]
- Tremors
  - Twitching
  - Hallucinations
  - Agitation/Irritability
  - Overactive reflexes
  - Loss of appetite
  - Increase of appetite
  - Sore throat
  - Runny nose
  - Nightmares
  - Loss in sexual ability, desire, drive, or performance
  - Joint pain, stiffness, or swelling
  - Dry skin
  - Restlessness
  - Hair loss
  - Hair growth

**14. If the benefits included treatment or relief from your PBC symptoms, which of the following risks or side effects would you accept?**

- Dizziness
- Itching
- Depression
- Anxiety
- Mania
- Suicidal thoughts or ideation
- Nausea
- Vomiting
- Diarrhea
- Drowsiness
- Dry mouth
- Insomnia
- Constipation
- Headache
- Rash
- Kidney damage
- Liver damage
- Pancreatitis
- Eye damage

**15. What is your age?**

- 0 - 18
- 18 - 30
- 31 - 45
- 46 - 60
- 61 - 75
- 76 - 90
- 91+
- Prefer not to answer

**16. What is your biological sex?**

- Female
- Male
- Prefer not to answer

**17. What is your gender identity?**

- Woman
- Man
- Transgender Woman / Trans Feminine
- Transgender Man / Trans Masculine
- Non-Binary / Genderqueer / Gender Fluid
- Two Spirit

**18. From where would you place your genetic heritage? (We are looking to explore genetic aspects to Urso response, symptom burden, etc, so we are looking at racial genetic aspects, as opposed to cultural or ethnic history.)**

- Indigenous North America
- Central America
- South America
- Europe
- Middle East
- Northern Asia
- South West Asia
- South East Asia
- Indigenous Australasia
- Mixed
- Not sure

**19. Are you interested in speaking to the U.S. FDA, pharmaceutical and biotechnological representatives, academics, clinicians, etc. on behalf of the PBC community, e.g. during the Global Liver Institute's Externally-Led Patient-Focused Drug Development Forum on February 4, 2022? The meeting will be virtual and speaking slots will be approximately five minutes. If yes, please provide a brief summary of your PBC journey and your email address. This question will not be cross-referenced with any other question so your data will remain anonymous.**

- Yes [free response]
- No

**20. What country do you live in?**

[Drop down selection box of countries]






**21. What is your state or province?**

[Drop down box of states and provinces]

**End of Survey**

Global Liver Institute (GLI) is a patient-driven 501(c)3 nonprofit organization headquartered in Washington, DC, with offices in the EU and UK, founded in the belief that liver health must take its place on the global public health agenda commensurate with the prevalence and impact of liver disease and the importance of liver health to well-being. GLI promotes innovation, encourages collaboration, and supports the scaling of optimal approaches to improve research, care, and policy. By bringing together more than 200 community-based, national, and international organizations across its Councils, Campaigns, and events, GLI equips advocates to identify and solve the problems that matter to liver patients. Follow GLI on Twitter, Facebook, Instagram, LinkedIn, and YouTube.

*Global Liver Institute (GLI) gives the FDA the necessary permissions to link this resource from the FDA website, and the posting of this resource will not violate the proprietary rights of others.*

- globalliver.org 
- info@globalliver.org 
- @globalliverinstitute 
- @GlobalLiver 
- Global Liver Institute 

**Point of contact:**  
Royze Cachero  
Program Manager  
Pediatric & Rare Liver Diseases  
Global Liver Institute  
pedsrare@globalliver.org





