CHOLESTATIC PRURITUS ASSOCIATED WITH PBC: UNDERSTANDING UNMET PATIENT NEEDS AND TREATMENT STRATEGIES

Editor's Note: This is a transcript of an online course released in December 2024. To obtain credit for participation, CLICK HERE.

Faculty

Alan Bonder, MD
Medical Director of Liver Transplant
Beth Israel Deaconess Medical Center
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Kris Kowdley, MD
Director, Liver Institute Northwest
Medical Director and Senior Scientific Advisor, Velocity Clinical Research
Professor, Elson S. Floyd College of Medicine
Washington State University
Seattle, Washington

Introduction

Kris Kowdley, MD: Let's begin with a discussion of primary biliary cholangitis (PBC). This is an immune-mediated disease that targets the small ducts within the liver and results in chronic intrahepatic cholestasis. This autoimmune destruction of the small bile ducts is associated with damage to the bile ducts and leakage of bile acids into the liver parenchyma that can cause toxicity to hepatocyte membranes and may recruit secondary inflammatory cells to cause further injury.

The incidence of PBC is estimated to be about 2.75:100,000 persons in North America. It's a predominantly female disease with a female to male ratio of 5:1. And, in the absence of treatment, there's a significant impact on transplant-free survival. In patients who are untreated, 59% will survive 10 years, and only 32% of patients may survive at 15 years. The introduction of ursodeoxycholic acid (UDCA) has had a major positive impact on natural history of PBC and, with treatment, you can see that the 10- and 15-year survival is significantly improved. Despite the progress that's been made, we still have a need for additional second-line treatments and our treatment goals are gradually evolving so that we are hoping to achieve biochemical remission in a substantial proportion of our patients.

From the standpoint of disease modification, we've made progress, but PBC can significantly impact quality of life due to fatigue, pruritus, right upper quadrant pain and Sicca syndrome.

Alan Bonder, MD: When we look at the epidemiology of pruritus associated with PBC, a study done by the United Kingdom PBC (UK-PBC) group showed that 74% of patients experience some type of itching, 35% reported persistent itching through their entire disease and some of them, up to 12%, complain of severe itching. Also, 75% of patients complain of itching even before they were diagnosed with PBC and some of them actually improve with the destruction of the bile ducts and you have progression to cirrhosis. Again, this is just pointing out that these are all epidemiological studies.

This is really a very important study done by Dr. Marlyn Mayo at UT Southwestern where she looked at the burden of itching in 6 really important parts of our quality of life. This is the PBC-40 questionnaire that patients with PBC answer on a visit-to-visit basis when seeing a PBC expert. As you can see, you address itch, emotional symptoms, fatigue, social and cognitive issues. And she divided them into 3 groups: no itch, mild itch and clinically significant itch. And, as you can see, those patients who had clinically significant itch had worse scores, I mean high scores on their PBC-40 from the itch, the emotional, the symptoms, the fatigue, the social and the cognitive. This is really such an important symptom that we need to address to improve the quality of life.

Animation Voiceover: The pathophysiology of pruritus in PBC is thought to be mediated by 4 pathways and possibly others. The first is an excess of bile acids in tissues leading to activation of the Mas-related G protein-coupled receptor X4 (MRGPRX4) and possibly the transmembrane G protein-coupled receptor 5 (TGR5), which are expressed in sensory neurons and mediate itch-related signals. Second, the enzyme autotaxin (ATX) converts phospholipids to lysophosphatidic acid in cell membranes, which then activates the transient receptor potential cation channels A1 (TRPA1) and V1 (TRPV1) found on C-fiber nerve endings. Once activated, these channels increase the itch sensation and release pruritic cytokines. Third, the farnesoid X receptor (FXR) is overstimulated in PBC, which leads to an

increased level of the pruritic cytokine interleukin-31 (IL-31), which is a known mediator of itch. Fourth, the level of circulating opioids is increased in patients with liver failure, resulting in increased stimulation of the mu-opioid receptor, which is known to potentiate the itch signal.

Diagnosis and Monitoring

Alan Bonder, MD: I want to just take a moment to go over this interactive model of how itching or pruritus develops in patients with PBC. How does that present? We know that the itch from PBC is usually in extremities, in the palms and the soles. Sometimes it can be generalized, but the kind of pathopneumonic part of this itching, you do not develop any lesions. It usually follows a circadian rhythm with higher intensity in the evening or night hours and one of the interesting parts of this disease can wax and wane. Some patients exhibit severe itching and, as they go through their disease activity, this disappears and then will come back again, which makes it harder to treat.

Let's just take a step back and look at how we diagnose PBC. Currently, based on the American Association for the Study of Liver Disease, you need 2 out of the following: 1, you need a cholestasis based on elevation of the alkaline phosphatase, number 2, you need the presence of antimitochondrial antibodies or other PBC-related antibodies. And if you don't have 1 of these, then a biopsy showing nonsuppurative destructive cholangitis and destruction of the interlobular bile ducts would show that this patient has PBC.

The diagnosis of itching in patients with PBC could be quite difficult and I think when we're assessing itching, the first thing we need to ask ourselves is do you have any skin lesions. And if you do, is it related to PBC. I think using the help of a dermatologist will help us to kind of either biopsy to describe it a little bit more. When you see itching with a kind of nonlesions in the skin, that's something we need to kind of look a little more deeply and to other related issues that concomitantly appears with PBC, such as, for example, neurological conditions, psychiatric conditions, endocrine conditions. And, finally, we need to make sure we exclude everything else that can cause itching in patients with PBC before we actually determine that this itching is related to the condition.

This is a very subjective symptom and, as it's very subjective, it's hard to assess from a patient, actually, and provider perspective how to give this symptom a scale. In the last couple of years, we have developed some assessment tools to make this more objective, so we can basically get it treated with the right medications. On the left-hand of the slide, you can see the 2 most common scales that we use in clinic. The first one, the Worst Itch Numerical Rating Scale (WI-NRS), which basically goes from 0 to 10. When you ask the patient, 0 is no itch, 10 is unbearable itch and the patient gives you a number. The next one, which is the Visual Analog Scale, you put a chart in front of the patient and the patient will point out exactly what the patient feels the itch is causing issues. On your right-hand side you see it's an unbearable itch, and the left-hand side you see where there's no itch.

And finally, we have other tools that help assess if patients are having itching. The PBC-40 is the best example for that. This is a validated questionnaire and score that has been used in research in patients with PBC where you ask 40 questions that emphasize the quality-of-life aspects of itching. When you assess itching in the PBC-40, they ask about is it disturbing your sleep, if scratching has made the skin raw, if you have any embarrassment going out because of stigma? All those things help us really put the symptoms into a right objective context so we can give patients the right treatment.

What we do clinically is, once the patient gives us an objective score of their itching, I think we should bring those patients back to clinic in 2 to 4 weeks and reassess their itching once we have given the patient some treatments. If we don't see any improvement in their itching, Therapy should be advanced or escalated, which will be talked about in detail in the next couple of slides.

Treatment Overview

Alan Bonder, MD: What are our goals? I want to mention that an important goal is to recognize, as I mentioned before, up to 70% to 80% of patients come in with symptoms of itching, so the first thing to find out if those patients are really having severe symptoms. And once they do, we need to make sure that we reduce disease burden. We need to give them the right treatment so they can improve quality of life. We need to minimize treatment-related adverse events. And finally, we need to prevent their PBC progressing to advanced liver disease, or dying, or needing a liver transplant.

This is a really great review by Cynthia Levy from the University of Miami where she looks at 2 things that we focus on when we're treating patients with PBC. Currently, physicians are really worried and occupied about disease activity. When you look at the left-hand side of the slide, as we see with diagnosis of PBC, we want to put them on the right treatment and we're focusing on disease activity, the alkaline phosphatase (ALP), total bilirubin, and the response to therapy. But I think we need to change the way we look at patients with PBC and we need to make sure that quality of life and symptoms are also part of their assessment on a month-to-month basis. For example, when we look at therapies, they look at liver tests, fibrosis and symptoms, but also we need to make sure that the quality of life gets assessed as part of their day-to-day routine so we can give them the right treatments.

What do we use to treat patients with PBC? UDCA is the first-line therapy that gets the disease under control between 60% to 70%. And what I've seen multiple times is patients come to me saying that the UDCA was given not only for their disease, but also for their itch. And I want to emphasize that UDCA does not really treat, at all, their itch.

We have new therapies available. The fibrates or the peroxisome proliferator-activated receptor (PPAR) agonists, specifically bezafibrate, which is currently unavailable in the US, improved biomechanical markers and relieved the itch in PBC. Currently in the US, we are using fenofibrate which has been okay treating mild to moderate itching. From 2016 to 2023, the only second-line therapy was obeticholic acid. We know that obeticholic acid's main side effect is itching, depending on the dose. For example, in people using 5 mg, up to 50% will complain about itching and in people using the 10 mg, up to 70% will have severe itching and unfortunately, this is a side effect that will make you stop using those therapies.

And fortunately for us, in the last couple of months we've got 2 medications approved by the FDA. This is elafibranor and seladelpar which are very specific peroxisome-proliferated PPAR agonists that have been shown to treat disease activity as well as improve the itch.

Kris Kowdley, MD: To highlight some key concepts in managing itch in PBC, ursodeoxycholic acid, is not effective for pruritus. Individual patients may report that pruritus is improved or may even report pruritus has worsened with UDCA therapy. Obeticholic acid clearly is associated with itch in a dose-related manner and patients who start at 10 mg, 10% of those patients have to discontinue therapy due to itch, with a much lower percentage discontinuing due to itch among those who start at 5 mg and titrate up to 10 mg. We can manage the pruritus with OCA with appropriate dose escalation and mitigation of symptoms, but it remains not an attractive therapy for patients with PBC who already itch. Fibrates, not FDA approved, may have a favorable effect on pruritus. PPAR agonists, which are FDA approved, may improve liver biomarkers as well as improve pruritus.

But undoubtedly, pruritus should be assessed with each office visit using, if not validated tools, at least a visual analog scale with an attempt to quantify the pruritus from the patient's perspective and to evaluate the impact on quality of life. A stepwise approach with close follow-up, which can be done by telephone and doesn't require a patient visit, should be taken to validate the pruritus symptoms in patients with PBC and to try to improve symptoms.

Current Treatment Options

Alan Bonder, MD: A key question that I get asked from patients is, besides medications, is there anything else that patients can do for general management? I usually tell them to avoid heat, frequent bathing with hot water, ice packs (because that will actually irritate the skin), skin contact with irritants such as soaps, consumption of large amounts of hot and spicy foods, hot drinks or alcohol, tight clothing or wool (which will cause itching), scented detergents, and extensive rubbing of the skin. For example, I ask them to cut their nails. Finally, try to see if they can avoid psychological factors that will cause stress and that will make them again think about the itch.

I do ask them to use nonalkaline soaps, use lukewarm water or bathing less than 20 minutes, use a moisturizing cream, use topical agents with anesthetic effects, wear soft, loose and permeable clothes, trim their fingernails, and finally try to get them into relaxation techniques or autogenic training to disrupt any itch-scratching cycles.

This is one of our papers that we published in 2017 with Dr. Trivedi who's currently now at Cedars-Sinai. We looked at all the different therapies that had been published for itching. And again, I want to point out this is 2017, but I want to make sure that we looked at it as a stepwise approach. For example, the use of antihistamines is not effective. We

know that they're not effective and again, none of our current guidelines recommend using antihistamines. Step 1 is using cholestyramine, the bile acid binder. The problem with using cholestyramine is drug-drug interactions, the taste, and finally the side effects. When you get into moderate to severe symptoms, step 2 and step 3 are my favorites. What I've seen in clinic is rifampin is one of the most effective therapies that we have out there for treating and getting itch under control and has minimal side effects, as long as we monitor liver tests. And just remember, once we start 1 of those therapies, bring those patients back in a couple of weeks to reevaluate them or review those tools or questionnaires to see if the itching has improved.

Kris Kowdley, MD: Fibric acid derivatives, PPAR agonists and ileal bile acid transport (IBAT) inhibitors may all help cholestatic pruritus. We believe that antihistamines, on balance, do not provide benefit. UDCA may exacerbate pruritus and OCA definitely can exacerbate pruritus in patients with cholestatic itch.

Let me now talk about some of the new therapies that have been approved recently, this year. I mentioned the PPAR agonists, so elafibranor is a PPAR-alpha/delta dual agonist. This was studied in a phase 3, double-blind, placebo-controlled trial at a dose of 80 mg a day. Patients with PBC who had an inadequate biochemical response or unacceptable side effects to UDCA were included in the study. And the primary endpoint for the ELATIVE trial as for the upcoming RESPONSE trial which I'll mention are similar to the original POISE trial of OCA and all these studies have used the primary endpoint of a composite biochemical response and that is how many patients or what portion of patients treated with drug compared to placebo achieved a reduction of serum alkaline phosphatase to less than 1.67 times the upper limit of normal with at least a 15% reduction from baseline and maintained a normal total bilirubin level.

Secondary endpoints that have been evaluated in the ELATIVE trial and subsequent trials include the alkaline phosphatase normalization and change in pruritus intensity using the Worst Itch NRS score at 24 and 52 weeks.

And here are top line results from the ELATIVE trial. 51% of patients treated with elafibranor compared to 4% on placebo achieved this composite biochemical response with a 47% placebo-corrected difference. When you look at Least Square Mean change and Worst Itch NRS, you can see there's a trend towards improvement with elafibranor compared to placebo, but it did not achieve statistical significance. And when you look at itch domain in the PBC-40 and 5-D itch, there does appear to be a differentiating trend in that PBC-40 and 5-D itch scores seemed to improve to a greater degree with elafibranor compared to placebo in treated patients.

With elafibranor, there was a similar incidence of adverse events between the 2 groups from a safety perspective. Most were mild or moderate. One different side effect that can be seen, as expected with this class of drugs, is elevated creatine phosphokinase (CPK) and muscle injury which were more common in patients taking elafibranor compared to placebo, and there were some discontinuations because of elevated CPK. Fractures and GI symptoms are the other most commonly associated side effects associated with elafibranor therapy and I would recommend that the interested participant review the full details in the prescribing information for risks and benefits associated with safety.

Now, seladelpar was studied in a phase 3 trial as well, entitled the RESPONSE trial. This was a phase 3, double-blind, placebo-controlled trial comparing 10 mg of seladelpar to placebo. The entry criteria were very similar as in the ELATIVE trial, in fact they were identical with regard to patients who had an inadequate biochemical response or were intolerant to UDCA. And the primary endpoint was also similar in terms of the proportion of patients achieving an alkaline phosphatase less than 1.67 times the upper limit of normal with at least a 15% reduction and maintaining a normal bilirubin with secondary endpoints also focused on normalization of alkaline phosphatase and improvement in itch scores.

And you can see here that a 41.7% difference in placebo-corrected response was observed with seladelpar compared to placebo, with 25% achieving normalization of alkaline phosphatase and a statistically significant difference in terms of improvement in itch in those with moderate to severe pruritus at 6 months compared to placebo.

Safety in the seladelpar trial was also assessed and was similar to the ELATIVE trial. The incidence of adverse effects was similar between the 2 groups. There were more pruritus cases reported in placebo with headache and GI issues being reported more commonly with seladelpar.

There were no treatment-related serious adverse events and adverse events leading to discontinuation of therapy were rare and similar between the 2 groups.

Now, a novel approach to treating pruritus in cholestatic liver diseases is with ileal bile acid transport (IBAT) inhibitors. Bile acids undergo enterohepatic circulation. There's a specialized portion of the small intestine in the terminal ileum that contains an area where bile acids are taken back up into the circulation and reach the liver, and that comprises the enterohepatic circulation as shown on this slide. IBAT inhibitors block reabsorption of bile acids in that specialized terminal ileal area leading to disruption of the enterohepatic circulation and therefore excretion of bile acids in the stool. Inhibition of IBAT results in an increased amount of bile acids being delivered to the colon as opposed to the enterohepatic circulation and fecal excretion of bile acids.

Maralixabat and odevixibat are 2 IBAT inhibitors in development. These have been approved to treat cholestatic pruritus in patients with Alagille syndrome and progressive familial intrahepatic cholestasis (PFIC). There are trials that are underway for treating pruritus associated with PBC, but approval of these agents for PBC-related pruritus has not yet happened.

We may continue to use nonpharmacologic therapies, such as phototherapy, plasmapheresis, albumin dialysis, nasobiliary drainage. Liver transplantation has been used in severe cases of pruritus associated with cholestasis and it always remains important for us to continue to educate patients for optimum management of skin hygiene and mitigation of symptoms to the highest degree possible.

Alan Bonder, MD: Phototherapy, is basically a mechanism that we don't know how it works. We think that it helps metabolize from an indirect to direct bilirubin, but we really don't know. Studies are observational. One small cohort of 13 patients who already failed standard treatment with either cholestyramine, rifampin, or naltrexone and when these patients went into phototherapy, their visual analog score decreased after a mean of 8 weeks and 26 treatments. This was a generally well-tolerated therapy without any major side effects.

Plasmapheresis is a little bit more invasive. We know today that there are certain inflammatory cytokines or inflammatory markers that go into the circulation that will cause the itching. In theory, removing pruritogenic cytokines will treat the itching. This is another really small study of 17 patients who used plasmapheresis. Those patients were refractory to itching that did not respond to cholestyramine or rifampin. Patients had an average of 2 admissions and an average of 2 to 4 procedures, and you can see that the NRS score decreased by 5 with a mean decrease from 8.3 to 3.1.

Another type of therapy that we have available is albumin dialysis or molecular adsorbent recirculating system (MARS). Another observational study of 20 patients who got a total of 28 treatments where the VAS score decreased by 72% immediately after treatment and 51% at 1 month. It is considered safe, well tolerated, but unfortunately is very expensive and not broadly available.

Another invasive treatment option for itching is nasobiliary drainage. A small study of 27 patients received, through endoscopic procedure, the placement of a nasobiliary drain. Nasobiliary drainage reduced the itch in 89.6% of the cases. The VAS score decreased from 10 to .3, with a median duration of the effect of 50 days. Unfortunately, there were some adverse events with the placement of this tube with pancreatitis. And this is again, not a widely used therapy.

And finally, I do want to mention about liver transplantation. For those patients who are not able to get their symptoms under control despite doing everything possible for them, liver transplantation is still an option for their PBC. Unfortunately, symptoms don't have any exception points. At this point, if those patients need a liver transplant, we really explore a living donation or getting on the list to see if they can get an offer.

And finally, I want to bring up the most important point about itching, which is patient education. Patient education is key. Number 1, we need to make sure the patients communicate to their doctors about this symptom. We need them to know that some itch remedies like antihistamines that we used to use, really don't work. Itch tends to be worse in the evening, so of course disrupting the sleep. We have really good medications. I told you that my preference is using rifampin or naltrexone because I think that really relieves moderate to severe itching. We need to go over general measures of itch relief. In those people who really scratch a lot, make sure that you watch for signs of infection. And finally, try to keep a journal or log about how your itch is doing. Again, it's so important to

assess itching with those tools every 2 to 4 weeks, assess with the scores so that both the patients and their physicians really understand if treatment or therapies are really working.

Kris Kowdley, MD: The key concepts that we are trying to communicate here are the efficacy of treatment options must be weighed against ease of use and side effects. And regular and close management of pruritus or at least assessment of pruritus and definitely evaluating the impact of pruritus on the patient's quality of life and overall functioning is really key for us to be able to achieve patient-centered goals. There is some encouraging evidence that the recently approved PPAR agonists may provide benefit for some patients with PBC while also treating the PBC. And so, in this regard, may have disease modification but also symptom alleviation as goals that we can accomplish. But, even with the PPAR agonists, statistically significant improvement in itch is not seen until 6 months of therapy, as in the RESPONSE trial. There is a need for additional therapies, and the concept of using IBAT inhibitors for treating cholestatic itch is very encouraging, particularly based on the data seen with PFIC and Alagille syndrome.

Investigational Therapies

Kris Kowdley, MD: Linerixibat has been studied and recently just completed a phase 3 trial. The phase 2 GLIMMER trial was a multicenter, double-blind, randomized parallel group study. 147 patients with PBC and moderate to severe pruritus were enrolled. Those who had a Worst Itch NRS score of greater than or equal to 3 were randomized 3:1 to 12 weeks of treatment or placebo at doses of 20 mg, 90 mg or 180 mg once daily, or 40 mg, 90 mg twice daily, or placebo. The primary endpoint was a change from baseline in Worst Itch NRS with a proportion of patients achieving a score of less than 4 as being one measure. Reduction from baseline of more than 30% or a 2-point improvement as another measure with secondary endpoints including a mean change from baseline for all 6 domains of the PBC-40.

And here are the results from the GLIMMER trial. You can see that all groups, including placebo, improved, and the change in monthly itch score does appear to be dose-related and potentially provided the basis for the GLISTEN phase 3 trial.

The efficacy for the GLIMMER trial is shown on this slide. The group that received 40 mg twice a day showed significant improvements compared to baseline at week 16 in PBC-40 itch, the social and emotional domains and itch scores, 5-D itch scores and sleep scores improved compared to baseline in all groups, including placebo. There was no consistent or clinically relevant improvement in fatigue scores, however, but there was a high concordance between improvement in itch and improvement in sleep.

From a safety perspective, drug-related adverse events occurred in 19% of the placebo group and 31% to 78% of patients in the linerixibat groups. As expected with IBAT inhibitors, the main side effect is diarrhea, and the most common adverse events were diarrhea and abdominal pain. This was dose-related with a dose response relationship observed for diarrhea and abdominal pain. Treatment-related adverse events that led to discontinuation of therapy were diarrhea in 10 patients, abdominal pain in 5 and 1 patient discontinued therapy due to abnormal liver tests.

Volixibat has been studied in a clinical trial called VANTAGE. This is a phase 2b study that was just presented as a late-breaker poster at the AASLD meeting and this study compared volixibat 20 mg daily, 80 mg daily or 20 plus 80 mg daily compared to placebo. The primary outcome was a mean reduction in itch score based on Adult ItchRO scale which is similar to a visual analog Worst Itch score. You can see that at 20 mg and 80 mg daily, as well as 20 plus 80 mg, there is a statistically significant improvement in itch compared to placebo with a difference between volixibat and placebo that was approximately -2.3 to -2.34 and this was statistically significant.

From a safety perspective, the adverse events were as expected. They were similar between the 20 and 80 mg treatment groups with mild to moderate diarrhea being the main symptom with 1 patient discontinuing due to diarrhea and there were no clinically significant changes in liver function tests.

The key concepts with ileal bile acid transport inhibitors are that these agents show promise in providing another tool to treat patients with pruritus associated with PBC, but of course no therapy using IBAT inhibitors at this point is approved, although we are very optimistic based on the recently completed GLISTEN phase 3 trial as well as other trials underway that IBAT inhibitors may turn out to be an attractive therapy for cholestatic itch.

Interprofessional Patient Case

Alan Bonder, MD: I'm going to review a regular case scenario that will show up in our clinics. This is a 38-year-old Hispanic female who presents with complaints of fatigue and itching that started 18 months ago. She was diagnosed with PBC after an extensive workup and started on UDCA. Her liver biomarkers have improved, but she still complains of persistent itch. She is tearful as she describes not having energy for activities with her 2 young children because of poor sleep due to nocturnal severe itching. She has failed a trial of gabapentin and sertraline.

On physical exam, we see severe excoriations on the palms of her hands with swelling and redness present and her vital signs are within normal limits. Her past medical history includes type 1 diabetes, hypertension, both well controlled with medications. She is on UDCA 600 mg twice a day, obeticholic acid 5 mg daily, an insulin pump and she takes creams with hydrocortisone for her itching. When we assess her itch scores, her NRS is 8, her PBC-40 is pretty high and her labs show an alkaline phosphatase of 150 U/L, an aspartate transferase (AST) of 40 U/L, an alanine aminotransferase (ALT) of 50 U/L, bilirubin at 1.5 mg/dL and a glycated hemoglobin of 7.2%.

The question is how can PBC specialists and primary care providers work together to enhance patients' outcomes. And I think the most important thing is to recognize it. Now we know that the patient has itching and looking at her medical history, we know that the patient is taking a medication that can cause severe itching in up to 50% of patients. Also, primary care providers should be educated about the new therapies and their side effects because both primary care providers and specialists should know about the side effects.

Kris Kowdley, MD: This case really highlights how we need to come together, both from a standpoint of being a PBC specialist but also primary care provider, to improve patient outcomes, because this is a patient whose hemoglobin A1C needs attention, who is on insulin for diabetes, on obeticholic acid for second-line therapy, which is undoubtedly also contributing to the itch. It takes a village to help care for these patients to achieve both quality and quantity of life as much as possible.

And we always need to keep in mind that we need to support our patients with regard to mental health, because the psychologic and emotional impact of pruritus can be devastating for many patients. I always keep in mind and always am open to recommend to the patient an evaluation for mental health assessment with or without medication. This may include counseling, may include social work, or may include psychiatry.

Alan Bonder, MD: Is there a role for psychiatry? I think there is. Sometimes, patients, because of the symptom burden, develop depression, and are isolated. I do feel that there is a role for psychiatry in PBC. We've mentioned when we should ask our dermatology colleagues to be part of the therapy since those patients who have lesions, when we are not sure this is PBC or non-PBC related because sometimes a biopsy or sometimes some type of other therapies that they know better could make a difference.

Kris Kowdley, MD: We always need to wonder when should dermatology be consulted? Sometimes there are other dermatologic diseases that may also be autoimmune that may accompany the disease. If there's any lesion that is observed on physical exam, I think that would be 1 trigger for possibly considering a dermatology consultation and possible skin biopsy. And we always need to consider how can pharmacists and other healthcare professionals be added to the team to improve outcomes for our patients.

Alan Bonder, MD: Finally, how can pharmacists and other health professionals be leveraged to improve outcomes? This is so important because we prescribe a lot of medications. Pharmacists sometimes will know drug-drug interactions. For example, patients who are young, who are females who are taking rifampin and oral contraceptives (OCPs) or patients who are taking cholestyramine with all different medications. All those things need to be described and taught to the patient so we have the best outcomes for those patients. I do feel that pharmacists have a big role in taking care of patients with PBC and that we should encourage them to have this multidisciplinary care of our patients so we can have better outcomes for our PBC patients.