

Dr. Gideon Hirschfield from the University of Toronto discusses: **“What care should I expect to receive for my PBC?”**

So we brought to the group to come up with an integrated care pathway and this is just a slide to demonstrate and I'm going to go through this now for you in different stages and different levels of detail. It's not meant to be perfect, it's not meant to absolutely address everything that a patient has, but it's meant to sort of simplify the five stages of treatment from diagnosis, urso therapy, response to first-line therapy, treatment stratification, and the concept of second-line treatments, whichever ones you choose to have.

So, fundamentally we need in our care pathway that our patients have a very clear diagnosis. If you do not have a clear diagnosis in medicine, it is quite common to find that your treatment choices are muddled and do not always make sense. But, PBC is actually one of those diseases which is relatively straightforward to diagnose and actually we want to try to avoid complexity and focus on a clear diagnosis based on blood tests and antimitochondrial antibodies in around 90 to 95% of patients.

We then said, having made a clear diagnosis, everyone should be offered treatment with ursodeoxycholic acid. That doesn't mean everyone will take treatment with ursodeoxycholic acid, and it doesn't mean that everyone will tolerate treatment but everyone should be given the choice to take urso.

And then at the same time, have an assessment of their individual risk. Your risk of what's going to happen to your PBC is affected by many things: your age, your gender, how symptomatic you are. And we can stratify that risk into low, medium, and high and just understanding that actually trains your clinician to think about what to do for you and when to do it. It also helps you as a patient to make sure you ask, and so well have you considered this and have you considered that? So urso is first-line therapy, it is a weight-based therapy, 13-15 mg per kg per day and that's the therapy that we want everyone to get offered. Why? Because it works. I'm not saying that urso should stay the therapy forever. In the ideal world, in Nevada, in a COVID-free planet called Venus perhaps, we would treat PBC with amazing drugs that cured you. But for the time being, ursodeoxycholic acid is a very simple bile acid that mops up enough of that bile that's leaking out and causing a lot of irritation in your liver to make all patients live a bit longer and many patients live exactly the same duration as their neighbor.

But not everyone responds to urso in the same way, and not everyone gets an equal response. This is not a surprise, this is not different from any other disease, this is medicine. So your clinician and you need to know how you responded to urso, so that you can see what your risk is that you're going to do well, do averagely, or maybe not do as well as you like and you may run into needing new livers, etcetera.

Second-line treatment is there to change the risk of you developing late stage disease, licensed therapy (obeticholic acid), off-label therapies (fibrates, budesonide), clinical trials are also your

right, your choice, to help push the field forward and develop new drugs that will then become approved therapies and which may mean that PBC looks completely different in 10 years time.

So, my five key points for clinical care to take home, to bug your clinician about. Diagnose your PBC with confidence, you don't need more tests than you need because a clear diagnosis gets clear treatment. The first line treatment remains urso, in the future it may be something else, but everyone should be offered it. Ask about your symptoms and what can be done for your symptoms. We have good treatments for pruritus, we are working on treatments for fatigue. There will even be new drugs for pruritus in the next five to ten years potentially. Understand your risk and where you're going and then expect to be offered second line therapy, usually licensed therapy first but then there are options for trials and off-label treatments because you've had your risk stratified and your physician has said: "I can do better than leave you just on ursodeoxycholic acid."