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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Strategic Excellence: Mastering the Expanding ATTR-CM Therapeutic Landscape in Pharmacy Practice

Announcer:
Welcome to CME on ReachMD. This activity, titled “Strategic Excellence: Mastering the Expanding ATTR-CM Therapeutic Landscape in Pharmacy Practice” is provided by Medtelligence.

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Dr. Chen:
Once considered a rare condition, there's been some dramatic changes in the landscape for transthyretin amyloid cardiomyopathy, or ATTR-CM. We’re seeing increasing incidence in part due to heightened awareness and noninvasive techniques to recognize this disease earlier, along with some new data being released from clinical trials. So, what are some of the updates in this area and what are some of the treatment options available?

This is CME on ReachMD, and I am Dr. Hongya Chen.

Dr. Ferdinand:
And I'm Dr. Keith C. Ferdinand.

Dr. Day:
And I am Dr. Jennifer Day.

Dr. Chen:
So, Keith, can you share with us some of the updates in our landscape for ATTR-CM?

Dr. Ferdinand:
You know, we've come a long way. I've practiced cardiology for decades and I'm sure I missed patients who had ATTR cardiomyopathy. If you look back, we really didn't recognize it when we should. The red flags were there, we didn't recognize them. Bilateral carpal tunnel syndrome, patients who have a thickened heart on echocardiography, but it's discordant with their degree of hypertension. Patients who have an ECG or EKG, where their R-waves really aren't that high, despite on ECHO the heart being very, very thick. Along now, with noninvasive testing using nuclear medicine with technetium pyrophosphate and appropriate serum and urine protein electrophoresis, we can make the diagnosis.

You know, it's not just one disease. Amyloid fibrils come out as a tetramer and then they deposit in the carpal tunnel, in the heart. But there's also AL amyloid, which is a type of disease that comes from the bone marrow. And even within ATTR cardiomyopathy, it could be inherited, or it could be wild type. The wild type is seen especially in older men, although I think as we start to study more women, we're going to see that wild type, whereas inherited type is autosomal dominant, meaning that if you have it, there's a 50% chance that your children have it. The problem is it doesn't manifest itself until the old age. So, here's what we do. We now look at the red flags, those symptoms that I talked about, carpal tunnel syndrome, having a very thick enlarged heart, but the R-waves aren’t that bad, and hypertension never was that severe. We then add it with appropriate testing, technetium pyrophosphate scanning. We don't really have to do biopsy in many of these patients. We can make the diagnosis earlier and we now can intervene.

Now there's only one FDA approved treatment for ATTR cardiomyopathy, and that's tafamidis. It comes out of the liver as the tetramer, 4 units. Those units break apart. They end up causing amyloid fibrils that go to the carpal tunnel, goes into the heart and causes damage.

Tafamidis stabilizes those units. And perhaps by stabilizing those units, it stops the progression of cardiomyopathy. So, we now have the echocardiogram, with strain, the cherry on top, where you can see the strain, but the apex is preserved. We have the thickened heart. The R-waves are not as high, bilateral carpal tunnel syndrome, these red flags. And with appropriate noninvasive testing we don't have to do biopsy anymore in many cases. We can diagnose earlier, and we have at least one FDA approved therapy and that's tafamidis.

Dr. Chen:
Right. That's a very big change since years ago.

Dr. Ferdinand:
Yeah, like I said, I missed it, and we didn't have appropriate therapy. But now we've come a long way.

Dr. Chen:
Right. That's great.

Dr. Ferdinand:
Now, Hongya, let me ask you a question. We know on the molecular basis that ATTR comes out of the liver, it's the tetramer – breaks up, causes myofibrils – and they're different ways that we can approach this. What's the clinical trials evidence, on a molecular basis, how we can affect this disease?

Dr. Chen:
Right. Like you mentioned, TTR is produced in the liver and goes upstream, all the way to aggregate into amyloid fibrils. So, there are many ways we can stop this disease. But first, we can stop the TTR production in the liver and those we have silencers that we call them. There are four medications there, including inotersen eplontersen patisiran, and vutrisiran are currently available. And the 2nd mechanism, we can also stabilize the TTR. Like you said, when you dissociate into monomers that's when it gets dangerous and aggregates into the fibrils in amyloidosis. So, if we stabilize them like a key that kind of keeps the locks together, 4 units, then perhaps we can stop the progression of the disease.

In this category we have tafamidis, which was approved back in 2018, and now we have another similar stabilizer called acoramidis which just finished the clinical trial being evaluated by the FDA. And the 3rd part we can have amyloid fibril removers, which are more new, more recent and most of these medications are still in clinical trials.

Going a little bit into acoramidis just like tafamidis, it has positive signals in mortality, as well as cardiovascular events reduction. So, we are excited to see what the FDA says about that. In the silencer trials, patisiran was first approved for polyneuropathy in hereditary ATTR. And it was studied also in cardiomyopathy in APOLLO-B. Unfortunately, FDA did not find the results clinically meaningful to grant the expansion of the indication for cardiomyopathy. However, we have other silencers, like eplontersen as well as vutrisiran. They're both being studied in cardiomyopathy as well. So, we are also excited to see what those results show hopefully in the next few years.

Lastly, you know in the amyloid fibril remover we also are hoping to see good results there. We hope that by removing some of these fibrils in the organs, especially the heart, we can reverse some of the cardiac dysfunction that's causing patients to have heart failure. So, exciting things.

Dr. Ferdinand:
You know, it's surprising. Tafamidis, although it just stabilizes the tetramer, improves function, improves hospitalization and, boy, mortality. And there's not much we do in medicine to help people live longer.

Dr. Chen:
Right. Mortality is the ultimate goal.

Dr. Chen:
For those just tuning in, you are listening to CME on ReachMD. I'm Dr. Hongya Chen, and here with us today are Dr. Keith Ferdinand and Dr. Jennifer Day. We're discussing strategies to manage patients with ATTR-CM.

Dr. Ferdinand:
So, Jen, we've made a lot of progress. You're a clinical pharmacist. We have been able to show that we can even increase survival in some patients along with function. Tell me about your role as a clinical pharmacist in helping these patients with ATTR cardiomyopathy.

Dr. Day:
Yes. So, as you know, all of these medications that are available, which thank goodness we have them now. I remember previously, before 2018, we had nothing to offer these patients. So, it's exciting that we have so many options coming about. But all of them require

specialty medication management specialty pharmacy enrollment, pharmaceutical hub enrollments, lots of requirements outside the norm that take some time from prescribers to get patients started on access. And we know that the progression of this disease is so rapid in some cases that we need to get patients on therapy as quickly as possible. So, that's my role in our clinic is just, a lot of patient counseling, a lot of making sure prior authorizations get done, patients get started on appropriate therapies.

Dr. Ferdinand:
You know, in conditions like this, which can be very complex, especially with newer medications, it takes a team.

Dr. Day:
Absolutely.

Dr. Ferdinand:
So, we consider clinical pharmacists an important part of that team.

Dr. Day:
Absolutely. And you know, as you mentioned, I think a lot of times these patients, when treated with traditional heart failure medications, don't do very well. So, that can be another clue for us to take a look and see if the patient might have amyloidosis.

Dr. Ferdinand:
And you know, I wondered about those patients. We would put them on beta blockers, ACE inhibitors, ARBs, they'd get hypertension, fatigue, weakness, just didn't do well. Perhaps we were missing some cardiac amyloidosis.

Dr. Day:
Yes. Absolutely. I think that's true. Yeah.

Dr. Ferdinand:
So, the clinical pharmacist, along with the nurses, the physicians, the specialty doctors, all the part of a team. Do you have any examples, maybe a patient that illustrate how the team can work together? Some things that may help us understand how to approach these patients?

Dr. Day:
Sure, I can think of one patient in particular, Ms. TL. So, she was a 62-year-old Caucasian female referred to our clinic due to worsening heart failure symptoms. We found that she was in atrial fibrillation, which is also common, and so, she was started on beta blocker therapy for rate control. She was functional Class 3 to 4 at that time, and it actually declined once we placed her on beta blocker therapy with symptoms. Just did not tolerate the medication very well at all. And so, she came back in. We decided to go ahead and send her for a PYP scan. As you mentioned, it's so accessible and noninvasive, which is really nice to get that diagnosis. Patient did come back positive for ATTR-CM. She had I believe she was SPECT Grade 2 with a contralateral ratio of 1.63. So, we diagnosed her and started her on tafamidis, lowered her beta blocker, and referred her over. She underwent ablation for her Afib. And so, we now follow her every six months and she's functional Class 2 and doing very well.

As you mentioned earlier, it really doesn't take a long time on therapy to start seeing improvement in several of these patients. It's very encouraging.

Dr. Ferdinand:
You know what else is interesting? That atrial fibrillation that you mentioned, that's another red flag that we should look for, and those patients, regardless of their CHA_2DS_2-VASc score, need to be on anticoagulation.

Dr. Day:
Absolutely. Yes, sir.

Dr. Ferdinand:
Hongya, you're in Oregon?

Dr. Chen:
Right.

Dr. Ferdinand:
And I think you say you see patients who not only are in the rural areas, but even out of the state. How do you treat a patient over a long distance like that?

Dr. Chen:

Right. You know, it's challenging, you know, with all the travel and long distance. The access in these communities, who are outside of the metropolitan city, it's difficult. So we set up a multidiscipline clinic for amyloidosis that includes several specialties, including neurology, cardiology even hematology if we have bone marrow involved for light chain amyloidosis.

We also have sometimes GI doctors and kidney doctors. So, when we get a referral from a patient in the rural area we make sure they come in for maybe 2- or 3-days max with all the diagnostic imaging or testing they need to do, and then they can go see our doctors all in one day with all the appointments. It's almost like a one-stop-shop. And this really encourages the patient to come out because they don't have to go through multiple appointments to get the right diagnosis and right treatment. And after that we would diagnose the patient and whatever treatment options that were decided on, I will be helping them as a pharmacist. And all those can be done remotely. You know, we can send a prescription, we can send out an infusion clinic locally if that's what's convenient to them and therefore they can, you know, be treated appropriately even though they live in a rural area. So, that's a strategy that I think works for now, but we hope that in the future there will be a better system to really engage these patients who don't have the access that we do living in a big city.

Dr. Ferdinand:
Jen, do you have any problems with overcoming those distance problems in terms of access? What do you do?

Dr. Day:
We do a similar approach to Dr. Chen. I think it's very important in that initial visit with the patient, the initial diagnosis has been made, lots of patient counseling. We use lots of handouts, materials to give the patient to take home with them just so they have something to refer back to once they get out of the clinic. It's a lot to take in. And then from that point forward we can do a lot of communication by phone or by e-mail and continue to get them on their medications at home after all of that is completed. But, yes, the initial visit I just think is so important.

Dr. Ferdinand:
So, if you give them that handout, and it's you giving it to them and you educate them, that's called shared decision-making, you're actually increasing the chance that they're going to stay on therapy.

Dr. Day:
Absolutely. I think it's really important for the patients to buy into the whole process.

Dr. Chen:
Well, this has been a fascinating conversation but before we wrap up, Keith and Jennifer, do you have any take-home messages for us?

Dr. Ferdinand:
I have one important take-home message. The only diagnosis we will never make as clinicians is the one we don't think about. Amyloid cardiomyopathy is there. It affects the ability of a person to function, and it can decrease survival. We need to make the diagnosis and get patients to appropriate care.

Dr. Chen:
That's a great one, Jen?

Dr. Day:
Agree with you. I think working together and as a community, because again, the symptoms are so vague, so having everyone keep their eyes open for these things, getting good thorough histories on the patients and just having a low threshold for testing, for sure. Catching the patients earlier, working together to get them started on therapy as quickly as possible.

Dr. Chen:
Similarly, I think, you know, early diagnosis and early treatment is so crucial for this disease but don't give up. You know, I think when a provider encounters a difficulty, especially getting the medication, find help. Go to the centers that treat these patients commonly and ask for help. Hey, how do we do this? How do we help the patient get access when there are many local providers who do that, and collaborate with them.

You know we can get you the medicines for these patients and you just refer to us. We can collaborate and make it work. So, I think that's very important as well.

That's all the time we have today, so I want to thank our audience for listening in and thank you Dr. Keith Ferdinand and Dr. Jennifer Day for your valuable insights and expertise. It was great speaking with you today. Thank you.

Dr. Ferdinand:

Dr. Chen, thank you for all the great work you do with this condition. You've enlightened all of us, and I'm sure your patients benefit from your interventions.

Dr. Chen:
It's my pleasure.

Dr. Day:
Thank you, guys. It was really nice to talk to you guys and I hope that you have great success helping these patients in the future.

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