Transcript Details

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The BeAT Goes On: New Data on Improving Symptoms in HFrEF Patients Using Novel Device Therapy

Announcer:
Welcome to CME on ReachMD. This activity, titled "The BeAT Goes On: New Data on Improving Symptoms in HFrEF Patients Using Novel Device Therapy" is provided by Medtelligence.

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Dr. Abraham:
Despite guideline-directed medical therapy, or GDMT, many patients with heart failure continue to have worsening symptoms. But did you know that baroreflex activation therapy, or BAT, an implantable, FDA-approved, cardiac autonomic modulation device, improves exercise capacity, functional status, and quality of life? Join us today as we discuss BAT, the clinical trial data showing its sustained and durable benefits, and the benefits of its application in patients. This is CME on ReachMD, and I'm Dr. Bill Abraham.

Dr. Chahoud:
And I'm Georges Chahoud.

Dr. McCann:
And I'm Dr. Patrick McCann.

Dr. Abraham:
Dr. Chahoud, let's begin with you. Despite GDMT, many patients continue to have worsening symptoms and quality of life. Could you tell us why patients are still symptomatic and why residual risk remains? And how does this relate to BAT and its mechanism of action?

Dr. Chahoud:
Currently, the comprehensive, guideline-directed medical therapy remains foundational, and it's been shown to improve clinical outcomes, namely mortality as well as morbidity.

However, there are several limitations to guideline-directed medical therapy, that a lot of our patients do have problems with adherence to GDMT, and that's related to either medication cost, medication side effects, or even lack of efficacy. And about 1/3 of these patients remain symptomatic with minimal exertion, despite optimal target dose of guideline-directed medical therapy.

Furthermore, our GDMT has been shown to produce only modest improvement in quality of life and exercise capacity, barely about 2 to 5% change in exercise capacity, and that's totally different than what we've seen with device therapy, including CRT, which has had a greater effect on improving symptoms compared to GDMT.

Unfortunately, CRT therapy is currently indicated only in about 1/3 of patients with New York Heart Association Class II or III heart failure symptoms. BAT actually has a unique mechanism of action, because we all know that in heart failure patients, there is a decreased baroreceptive signaling which leads to an imbalance in the autonomic nervous system.

So the idea was maybe the baroreceptor activation therapy, as an extravascular device that can stimulate electrically the carotid

baroreceptors, could potentially increase the signaling to the brain, which will lead to a rebalance and modulation of the autonomic nervous system by inhibiting the sympathetic activity and enhancing the parasympathetic activity, leading to cardiac remodeling, reverse remodeling, increasing vasodilation, reducing the blood pressure, as well as enhancing diuresis. And we've all seen data to show that this has led to improved heart failure symptoms, quality of life, as well as functional capacity.

Dr. Abraham:
I couldn't have said it better myself. Patrick, any additional comments?

Dr. McCann:
I think there's a couple of things to point out in regards to medications. The side effects, most notably hypotension, but also the effect of comorbidities that reduces our ability to maximize GDMT thus lessening our ability to slow the progression of heart failure is substantial in the heart failure population.

Dr. Abraham:
So Pat, let's get specific here. Tell us the indications for BAT in heart failure.

Dr. McCann:
Sure. So patients that meet criteria for the device have NYHA class II or III heart failure symptoms, with an ejection fraction less than 35%, and an NT-proBNP less than 1,600, who are not candidates for CRT device, who are on maximally tolerated guideline-directed medical therapy.

Dr. Abraham:
A point well made, and you know, finally, I want to emphasize that unlike drug therapies which require patient adherence, device space therapies such as BAT don't. You know, once implanted, they operate automatically without the need for patient adherence or intervention.

Dr. McCann:
Absolutely. You know, now that we know what BAT is, and why it's needed, Bill, can you comment on the new data for BeAT-HF?

Dr. Abraham:
The BeAT-HF study was done under FDA's expedited access pathway, or the breakthrough devices program and was executed in 2 phases, a pre-market or pre-approval as well as a post-market or post-approval phase. During that first phase of the BeAT-HF study 264 patients, followed for 6 months, were evaluated for symptomatic endpoints such as quality of life and functional status and exercise capacity. And those endpoints were anchored against changes in NT-proBNP as an objective measure of improvement in the underlying heart failure clinical status. And then the second phase looked at long-term outcomes – the durability of safety and effectiveness, and also included a look at some clinical outcomes such as morbidity and mortality. And in that first preapproval phase of the BeAT-HF trial we demonstrated substantial improvements in quality of life, averaging about a 14-point between group difference in quality of life score, favoring treatment with BAT. To put that number into context, and as you've heard earlier regarding the limitations of pharmacological guideline-directed medical therapies, the average improvement in quality of life score with our drug therapies is a couple or 3 points. With device therapies such as and now demonstrated for BAT the improvements in quality of life are large. In addition, there was shown a very substantial improvement in 6-minute hall walk distance, averaging about 60 meters, and a 25% reduction in NT-proBNP levels at 6 months – a fall that is considered as a surrogate measure to be clinically significant, as it correlates with these other improvements in both symptomatic and clinical benefits.

So then, the second phase, the post-market phase of the BeAT-HF trial, was designed to extend these observations through the ongoing enrollment of additional patients on top of those original, phase 1 patients, looking at longer term follow-up, and also looking at clinical outcomes. And in that second phase of the BeAT-HF study, recently published, what we saw were sustained improvements in those symptomatic endpoints through 2 years. So, sustained improvements in quality of life. Sustained improvements in exercise capacity, or ability. Sustained improvements in New York Heart Association functional class ranking, and again, the demonstration of safety – long-term safety – with baroreflex activation therapy and the device-based system used to deliver it. In addition, while the trial missed its primary morbidity, mortality endpoint, additional clinical endpoints looking at, for example, the hierarchical composite of mortality, heart failure hospitalization and quality of life score demonstrated benefit to these patients.

[Insert Zile TBD]

Dr. Abraham:
So I would summarize, in general, that BAT is a therapy that is now shown to be safe. It produces durable effects on patient-centered endpoints, such as quality of life and functional status, and at least in one composite measure of clinical outcome, has also demonstrated benefit. And I think it really addresses that unmet need that Georges described earlier, in those patients who remain

symptomatic, remain disabled, despite their guideline-directed medical therapy, as a means to improve both patient-centered endpoints including quality of life and functional status.

Dr. Chahoud:
The interesting point that you alluded to from the BeAT-HF study, is that this therapy is not only safe and effective, but the treatment effects are durable in those patients with reduced EF [ejection fraction], and it mimics actually the results that we have seen previously, with the CRT data, from several of the clinical trials. It showed that the BAT therapy does improve quality of life as well as functional capacity to a similar extent as CRT therapy.

Dr. Abraham:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Bill Abraham, and here with me today are Dr. Patrick McCann and Dr. Georges Chahoud. We're discussing baroreflex activation therapy, or BAT, an implantable, FDA-approved, cardiac autonomic modulation device, the clinical trial data showing its sustained and durable benefits, and patient selection criteria.

Dr. Abraham:
So maybe you can tell us more about how this resonates with what you see in your patients in the clinic.

Dr. McCann:
We have really enjoyed BAT as a device for our patients, because it expands our options for heart failure care. Previously if patients could not tolerate medications, or they were still having symptoms despite medications, we had pretty limited options between placing them on inotrope therapy, or considering advanced therapies with mechanical support, or cardiac transplant. And unfortunately, as our population ages, those options aren't necessarily always the best options for our folks, and so with this device, we have been able to expand that window of opportunity for our patients with heart failure. In addition to expanding that window, we've seen a substantial improvement in their quality of life. Patients that come back into the clinic, that tell us that they are living, that they're not just only taking their medications, but they're feeling better now, that they're able to accomplish what they want at home, they're able to complete their activities without suffering from heart failure symptoms. And that's a wonderful feeling, to be able to provide that opportunity for our patients. So, in addition to all the other heart failure therapies that we have, I would say this one has made a most notable impact on how patients feel when they come back. And it's a very nice therapy, in that it doesn't require a substantial operation, it's a small procedure. Patients can go home the same day. The titration of the device is very simple for a clinic visit, and generally within 2-3 months, these patients are feeling much better, able to do more than they could have before the device, and are getting back to living.

Dr. Abraham:
You know, certainly there are some key takeaways here. We've heard about the unmet need that lays the foundation for BAT, and the BAT mechanism of action. And in particular, I think we've developed the concept that in these patients who remain substantially symptomatic despite optimized or optimally tolerated guideline-directed medical therapy that they want to feel better, and they need something else. And so I'd like to, I'd like to take off on those themes a bit, and just get some additional commentary from you. Georges, you want to start?

Dr. Chahoud:
It's important to screen the appropriate patients who qualify for these novel heart failure device therapies, and we've had it in our system a unique way where basically we're screening patients either through the heart failure disease management clinics, or our device clinics where these patients are housed, to make sure that we identify patients that are still symptomatic despite GDMT.

Or, that are not candidates for CRT but they do have an ICD and they are basically seen by our electrophysiology colleagues in the device clinics. And trying to perform a deeper dive on identifying which symptoms patients are still entertaining, and making sure that we identify and tease out those patients that will be appropriate for device therapy. What we've done in our system, is looking at place to refer those patients for our monthly novel device therapy conference, where these cases are discussed in a heart team approach, and we've seen a great, great stride and clinical improvement in patients' quality of life as well as functional capacity.

Dr. Abraham:
The other thing that you bring up, Georges, is you know, looking for these patients in the device clinic, the fact that many of these patients have ICDs, generally primary prevention ICDs. So we should be clear here that there is no contraindication to having barostimulation, or BAT, alongside an ICD, right?

Dr. Chahoud:
That is correct, for symptomatic relief there is no problem of implanting a second device that has been shown to improve quality of life as well as functional capacity in this matter that we've seen.

Dr. McCann:

Another area where patients can be recognized as a potential candidate would be during their hospitalization for heart failure, or if they've had a recent heart failure hospitalization, as oftentimes those patients experience NYHA [New York Heart Association] class III heart failure symptoms. One of the things we've noticed as we've used these devices more and titrated patients is that we are able to actually get them on higher doses, at times, of their GDMT following complete titration of the device, which I think has been great to marry the improvement in quality of life that we get from the device, but also that potentially have more of an effect on the longevity from the GDMT.

As far as how patients feel overall, consistently we have seen patients improve at least by 1 NYHA class, if not 2, and getting back to completing activities without any difficulty or any heart failure symptoms. And that's tremendous.

Dr. Abraham:
Well, fantastic. Well that's all the time we have today, so I want to thank our audience for listening, and thank both of you – Georges and Pat – for joining me and for sharing all of your valuable insights and expertise. It was really great speaking with you today.

Dr. McCann:
Thank you. It was wonderful to have this conversation.

Dr. Chahoud:
Thank you, and goodbye.

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