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2023 ESC Guideline Updates: Where Are We with Iron Deficiency?

Announcer:

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Dr. Rosano:

The 2023 Focus Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure was recently presented at the European Society of Cardiology Congress. So, how do these updates affect screening and treatment of iron deficiency patients with heart failure with reduced ejection fraction. This is CME on ReachMD and I'm Dr. Giuseppe Rosano.

Dr. Metra:

I am Dr. Marco Metra.

Dr. Savarese:

And I'm Dr. Gianluigi Savarese.

Dr. Rosano:

So, Marco, let's begin by discussing the guideline recommendations I just mentioned. What can you tell us about the recent updates of the ESC Guidelines, and how do they relate to treating and screening patients with heart failure and iron deficiency?

Dr. Metra:

Thank you, Giuseppe, for this interesting and important question. Actually, we have 2 new recommendations regarding iron therapy treatment of patients with heart failure and iron deficiency. And they were based on the publication of the more recent data from IRONMAN trial, but they regard – everything regarding iron repletion therapy for heart failure. One recommendation regards an indication for treatment of patients with iron deficiency, HFrEF, and HFmrEF with IV iron therapy with ferric carboxymaltose or ferric derisomaltose, after IRONMAN, to reduce heart failure hospitalization. This recommendation is a class IIa, and a level of evidence A recommendation. And this is very important because it's the first time that we extended the recommendation to iron therapy to all the patients with HFrEF and HFmrEF. Before we based only on AFFIRM-AHF, and it was only for after a heart failure hospitalization. But this comes with the data of IRONMAN and 4 meta-analysis data showed that the consistency of the beneficial effects of iron therapy in reducing heart failure hospitalizations in patients with iron deficiency.

The second recommendation, again, is for the first time we have a recommendation to iron therapy to improve symptoms and quality of life in the patients with iron deficiency and HFrEF and HFmrEF, and this is a class 1 recommendation, level of evidence A, because we have all the trials that consistently showed an improvement in symptoms and quality of life. So, we have a treatment that is recommended that improves symptoms and quality of life. It should be administered to reduce heart failure hospitalizations.

Dr. Rosano:

And the vast majority of data come from the studies with ferric carboxymaltose.

Dr. Rosano:

And, possibly all the data on quality of life and exercise capacity, they also come with ferric carboxymaltose. And, Gianluigi, what is your take on that?

Dr. Savarese:

Well, I would like to actually highlight how important is the recommendation regarding symptoms and quality of life. I think in heart failure we very much highlight importance of heart outcomes, but I think quality of life is very important for our patients. Several studies even show that patients do prefer living, actually, shorter but better. And, actually, now we have a treatment which clearly shows to improve quality of life and reducing symptoms, and this should really foster implementation of this treatment in clinical practice.

Dr. Rosano:

So Gianluigi, let me follow up and ask you another question. So, recent clinical trials with IV iron in patients with heart failure caused a shift in the definition of iron deficiency?

Dr. Savarese:

So, well the definition of iron deficiency in the update, it stayed the same, so nothing changed. Although, as we know very well in the IRONMAN, the definition of iron deficiency was slightly different, so we did add ferritin less than 100 and a TSAT less than 20%. Most of the evidence at the moment in the iron deficiency field considers the definition which has always been used, and before, I think it's completely consistent the fact that guidelines still record the same definition. And in any case, whether we do want to change the definition for iron deficiency, we should really think about having ad-hoc studies where we do correlate biomarkers with the level of iron depletion, even in the bone marrow. So, it's very much more complex than what we think when we consider a definition of disease.

Dr. Rosano:

I think, Marco, I would like to also hear your opinion. Is not important just the definition that may change slightly, may change a little bit country by country, but what is important is testing, because if you don't test, then you don't identify. So do you foresee any change in the future for the recommendation of testing – how frequently we should do it?

Dr. Metra:

No because, again, recommendations in the guidelines are based on the results of trials that give the evidence, and therefore with the current definition, we have the proof that the administration of ferric carboxymaltose is effective in improving symptoms, quality of life, and reducing hospitalizations. So, I don't think – so, you have to stay consistent with the definition used in the trials showing the efficacy, and it has worked.

Dr. Rosano:

For those just tuning in, you are listening to CME on ReachMD and I'm Dr. Giuseppe Rosano and here with me today are Doctors Marco Metra and Gianluigi Savarese. We are discussing the recent ESC Guidelines update and the totality of evidence of using IV iron when treating our patients with heart failure.

So, Marco, I really would like also to hear your thoughts on treating iron deficiency with IV iron in patients with heart failure. But first, do you consider IV iron to have a class effect, and does that heart failure status – heart failure with reduced ejection fraction, or mildly reduced ejection fraction – impact your treatment approach?

Dr. Metra:

Well, second question – I think it's – from this point of view, I think the trials have limited now the data to patients with reduced or mildly reduced ejection fraction. Also, I don't see a clear reason why iron treatment shouldn't work in patients also with preserved ejection fraction, but this is the current evidence. With respect of class effect or not also with other drugs, like SGLT2 inhibitors, we have again remained consistent with the results of the trials, and that the trials we have to date are the most recent with ferric derisomaltose, but otherwise we have all this large amount of data with ferric carboxymaltose. So, these 2 compounds remain in dose in the guidelines and remain the ones to use in clinical practice.

Dr. Rosano:

Yes, and also when we treat patients with IV iron, we have always to balance the benefits with also with the potential risks and IV iron replacement with ferric carboxymaltose have been proven to be completely, absolutely safe. So, Gianluigi, any additional comments on that?

Dr. Savarese:

Well no, I completely agree at the moment we have clear evidence in HFrEF and HFmrEF, but I agree with you, that probably HFpEF might be, you know, the perfect setting for treating patients with iron deficiency because these are patients who are frail and have medical morbidities and probably their iron deficiency might play a role, but at the moment we do not have evidence supporting this. But

hopefully it will come soon, and once again I think also this data confirm the fact that as for many other treatments for heart failure we show that what works in HF_rEF works also in HF_mrEF. And also, the evidence, I think, on iron deficiency and treating iron deficiency goes in the same direction.

Dr. Rosano:

Well, this has certainly been an enlightening conversation. But before we wrap up, can you each share one take-home message with our audience? Let's start with you, Marco. So, what's your take from this conversation?

Dr. Metra:

What I think the 2 recommendations are pretty good as a take-home. So treat iron deficiency in patients with heart failure to improve symptoms and quality of life and to reduce heart failure hospitalizations. And the drugs for which we have evidence are ferric carboxymaltose and ferric derisomaltose with a lot of data from ferric carboxymaltose and an ongoing trial, FAIR-HF2, to be ended soon and this will give data on some mortality, I hope.

Dr. Rosano:

Gianluigi.

Dr. Savarese:

So we should remember that iron deficiency is a very common condition. It's even more than 50% of patients with heart failure have iron deficiency. And this is a condition that you can treat, with treatments improving quality of life and reducing symptoms and improving outcomes, whether we make diagnosis of iron deficiency. And we do have evidence that screening procedures is still limited in patients with iron deficiency, for example, with data from Sweden showing that up to only 30% of patients receive screening. So my take-home message is like, we should screen, and we should make diagnosis and we should treat.

Dr. Rosano:

Yes. And it is important to have this update of the guidelines, but what also is important is that these recommendations are in keeping with the new data that have emerged because the HEART-FID study was at a *P* value that was significantly less than 0.05, so that statistically should be considered as a positive trial despite what the regulators set as a *P* value for regulators significance. So, I think overall we have very good evidence and backup evidence to support these new indications are very important for the quality of life of our patients with heart failure and effect on the hospitalizations. And those recommendations on hospitalizations have been long-awaited.

So, that's all the time we have today, so I want to thank our audience for listening in and Drs. Marco Metra and Gianluigi Savarese for joining me and sharing all their valuable insights. It was great speaking to you today.

Dr. Metra:

Thank you so much, it was our pleasure.

Dr. Savarese:

Thank you, Giuseppe.

Announcer:

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