Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.comhttps://cme.pace-cme.org/programs/cme/integrating-icosapent-ethyl-preventive-strategies-practical-guidance/16243/

Released: 08/23/2023
Valid until: 08/23/2025
Time needed to complete: 37m

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

Integrating icosapent ethyl in preventive strategies: Practical guidance

Hi, I'm Victor Aboyans. I'm a professor of cardiology in Dupuytren University Hospital in Limoges, France. I'm going to discuss how we can implement the use of icosapent ethyl in practice.

We know through the REDUCE-IT trial that if we use EPA in patients who have diabetes with one more cardiovascular risk factor or who are already in secondary prevention, we are able to reduce the cardiovascular event rates by 25%. Not only that, but we know also that these patients who can have repeated cardiovascular events have even a higher reduction of the overall cardiovascular events by 30%, so the use of this treatment could be really a benefit for these patients.

Having said that, then the question is how can we implement these major findings into clinical practice, and for that, we have to answer to several questions. What is the need in clinical practice? What do the drug agencies say after the publication of these results? What do the guidelines says about that? To whom should we propose this treatment in the real-life setting? Is this treatment well-tolerated or not? Should we have a special care or a special caution in some sub-group of our patients? Finally, do these results have a benefit regarding the cost-benefit ratio in our countries?

Post to address that, we'll start by the need and the concept of residual risk is very important. We know that using statins and other lipid-lowering drugs, we can reduce by 25 to 35% the risk of the patients, especially after a second cardiovascular event, but we still have almost 70% of residual risk despite a good LDL control. Back to some trials as the PROVE-IT TIMI 22, we know that patients who had already a well-controlled LDL cholesterol, if they had an increase in triglycerides by more than 150 mgs per deciliter, they have an increased risk of cardiovascular events in the future. Also in real life, we know that despite in patients who have already a well-controlled LDL cholesterol, almost 25% of these patients have a high level of triglycerides. The higher would be the triglyceride level, the higher is the risk of having further cardiovascular events.

What do the drug agency says and the European Medicines Agency following the public publication of REDUCE-IT? Clearly established and greenlighted the use of this treatment for patients who have a cardiovascular disease or have a diabetes with one additional risk factor, these patients should be already treated under statins and still have a triglyceride level above 150.

Regarding the guidelines, so back to the guidelines from the European Society of Cardiology and EAS in 2019, they first say statins for all patients and then if you still have an elevated triglyceride, you can use the icosapent ethyl on a daily basis, and this is a 2a recommendation made in 2019. Two years later in ESC 2021 guidelines on cardiovascular prevention, here again, patients who have a high triglyceride despite statins, can have a benefit of using icosapent ethyl and this is a 2b recommendation. Guidelines are in favor of using these treatments.

Now, if you go to the clinical trials, it is very important to highlight that all the trials using a mixture of EPA and DHA fail to show any benefit despite including almost 100,000 patients in these trials. While we have the newer trials, the REDUCE-IT and the JELIS showing a benefit and reduction in cardiovascular events in MACE overall, because they have used purified EPA.

Now, to whom can we propose this treatment in a real-life setting? I would focus on the secondary prevention and taking two situations, the patients who have a stable coronary artery disease, and in the clarify registry, it has been shown that almost 15% of the patients

would be eligible for the use of EPA on top of statins in that situation. After an acute MI, another registry, the FAST-MI registry showed that almost 12% of the patients would also be eligible for the use of these treatments.

Whether this treatment is well tolerated when we go to the comparison of the side effects between icosapent ethyl and placebo, where we can see that there are a bit higher rate of peripheral edema, 6.5% versus 5%, but also an increase in risk of atrial fibrillation, which was statistically significant. Looking at the landmark analyses, it seems that the risk increases after, let's say six to nine months and it is going to be significant at 16 months and then it would stay stable. The patients beyond this period wouldn't have an increased risk of having AF.

Looking at the serious bleeding, according to patients who have icosapent or placebo who had AF before or during the study, the bleeding risk was not increased in these patients. Regarding bleeding, we can say that there is a nearly significant increase in all bleeding events, but when we focus on the GI bleeding or central nervous system bleeding, or fatal bleeding, there was no significant difference. We can be reassured by the safety of these treatments. One particular situation can be after MI or after a coronary stenting when a patient is under DAPT and a new analysis on the REDUCE-IT has shown that this treatment is useful just after ACS and reduces MACE by more than 35%. Regarding the bleeding risk, so patients are already under DAPT, there are no increased risk of bleeding under EPA as compared to placebo. This is also reassuring information.

Is there any adjustment to do in elderly, renal failure, hepatic failure? No. We have no reason to adjust the treatment or the dose for these patients, and the safety is similar. Regarding renal failure, we can see this subgroup analysis showing that we have a consistent benefit of EPA independent of the level of GFR in the patients participating in the REDUCE-IT trial.

Regarding the cost-effectiveness, I am going just to show this single slide to reassure that in different countries with different health systems, in all of them, it has been shown that the use of icosapent ethyl is cost-effective according to their own criteria. You can also look at your own country data, but all in all, we see a cost-beneficial effect of this treatment in our patients.

If we want to summarize the situation and the use of icosapent ethyl in practice, we can say that the residual risk under statins remains substantial, especially in those who have a high level of triglycerides despite the use of statins. Around 15% of patients in secondary prevention would benefit from this treatment because they still have a high level of triglycerides. This is an estimation of almost 190,000 persons in France. You can do the maths for your own country. This treatment has now authorization from the European Medicines Agency and recommended by the ESC and the ESS as a 2a recommendation. This treatment is well tolerated. You have also only perhaps make some caution in patients at risk of atrial fibrillation, but there is no increased risk of bleeding even in elderly or patients who have renal hepatic failure or even patients under DAPT. It is cost beneficial. We have all the good reasons to use this treatment, so to tackle the residual risk of our patients.

Thank you very much.