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Keys to the Latest NLA Recommendations for Dyslipidemia Treatments

Alan Brown:
You're listening to ReachMD. This is Lipid Luminations sponsored by the National Lipid Association. I'm your host, Dr. Alan Brown. Joining me today is my good friend, Kevin Maki, who's a PhD and the founder and chief science officer for the Midwest Center for Metabolic and Cardiovascular Research and adjunct faculty in biostatistics in applied epidemiology at DePaul University in Chicago. You're one of the most thoughtful characters that I know. You have a great background in epidemiology, clinical trial design and been a trialist for many years. I know that you are one of the people involved in developing recommendations by the NLA to supplement the ACC/AHA guidelines. There's a fair number of folks who understand that these recommendations are being crafted. I wanted to take a few minutes and ask you a little bit about where we are in the process, what you hope to achieve by these recommendations and how they segue with the ACC/AHA guidelines that recently came out. With that introduction, I'd love to hear your thoughts.

Kevin Maki:
Thank you for that kind introduction. The NLA recommendations are in process, but they'll be available soon for everyone to read in the executive summary format.

Alan Brown:
Where is that going to be?

Kevin Maki:
That's going to be published in the Journal of Clinical Lipidology, the NLA's journal. And then following that, probably early next year will be a full report for part one that is going to include all of the background, rationale and more information than is included in the executive summary. But the executive summary covers the key elements of the recommendations and the recommendations are, in many ways, similar to those of the ACC/AHA but there are some material differences. Really, that derives from the way the evidence base was approached because the ACC/AHA used the Institute of Medicine model really focusing on what had been demonstrated in clinical trials. Our guiding principal was what we know about the process of atherogenesis and progression of atherosclerosis and what both clinical trials and epidemiology, genetic studies, mechanistic studies and so forth tell us so that I think the NLA recommendations include more expert opinion around areas that were either not covered by the ACC/AHA recommendations or guidelines and also places where there were some disagreements even within the panel and we came to a consensus about a reasonable way to approach patients in various categories given the imperfect evidence that we have available.

Alan Brown:

So in an ideal world, I guess my question for you would be where do you want to end up with this process? Before we get into the details, which I'm looking forward to discussing with you. Obviously, the AHA/ACC recommendations are out there and being used and promoted. Your recommendations add the expert opinion that I think even in their guidelines they suggested in those areas without clinical trial data one should turn to a lipid expert. So, I'm looking forward to seeing the recommendations. I'm sure they're going to add that expert opinion. For some of our docs, they want expert opinion. I understand the purity of going with just what the data shows. With that said, tell me where you, as a member of the writing group, would hope that the NLA recommendations will go and how should they be used? Then maybe comment on the simplicity of AHA/ACC recommendations, which makes it easy to digest and easy to remember. How will the NLA expert opinion and careful review of all of the science be used in addition to that relatively simple message?

Kevin Maki:
I think in part these recommendations will help both primary care clinicians as well as lipid experts address areas where the ACC/AHA recommendations are essentially leaving it open to clinical judgment. Many clinicians don't have time to go review the evidence and they want a concise summary of what experts in the field of lipidology believe is a reasonable approach. That doesn't mean that this is in any way replacing clinical judgment for individual clinicians but it's to help clinicians to understand what a group of NLA experts believed was a reasonable approach for patients. Ultimately, we hope that the NLA will be able to collaborate with ACC/AHA on future versions of guidelines and really get a seat at the table so that the NLA's viewpoints can be represented in upcoming sets of ACC/AHA recommendations.

Alan Brown:
I guess there are a couple of major issues to talk about. Number one is the institute of medicine recommendation the right way to do guidelines. Should we look primarily at prospective, randomized trials and very well done meta analyses and really not delve into expert opinion? That's just a philosophical question.

Then the second issue, the first steps of initiating treatment are adjudicated between the AHA/ACC versus your recommendations. I've only seen the brief release that was released in Orlando, so maybe you can give us a bit of a preview. In your opinion, as a trialist, as someone who teaches how to review data, is that the right way to do guidelines?

Kevin Maki:
I think everyone acknowledges that randomized clinical trials are the highest level of evidence and meta analyses and pooled analyses from results of randomized clinical trials are the highest level of evidence. But we have to keep in mind that clinical trials have limitations and limitations include things like studying groups that are not necessarily representative of the patient's often seen in clinical practice. Also, there are gaps in the clinical trial knowledge base because of the things like studying only fixed doses of medications as opposed to strategies such as treating to specific goal levels of atherogenic lipid proteins. So, while the Institute of Medicine approach has a place and I think you can make the distinction between guidelines and recommendations, guidelines taking the IOM approach to using only or recommending only what has been shown to be efficacious in randomized clinical trials, but I think that can be supplemented and probably needs to be supplemented by expert opinion that helps clinicians make decisions that they need to make.

If, as an example, you have a patient in clinical practice who's on statin therapy, maybe the highest dose of statin therapy tolerated, maybe the person has cardiovascular disease, does it make sense to add another agent if the person has an inadequate response to a statin? So, you have a patient with an LDL cholesterol level of 120, has coronary heart disease, is on the highest dose of statin tolerated. What is the evidence and the answer is we don't have great evidence from clinical trials to answer that. Therefore, expert opinion, we believe has a place. That's why these are called recommendation as opposed to guidelines because recommendations incorporate more of the judgment of experts based on what is known from epidemiology and the pathophysiology of the underlying condition.

Alan Brown:
If you're just tuning in, you're listening to ReachMD. I'm your host, Dr. Alan Brown and joining me today is Dr. Kevin Maki. We are

talking about the new NLA recommendations as a supplement to the AHA/ACC guidelines.

So the second part of my question was, how will the NLA recommendations appropriately interface with the AHA/ACC recommendations? I think everyone agrees that they did an amazingly careful review of the science. They answered three specific questions, which were the only three that I think there was a budget for. But they weren't crazy questions. What's the evidence for LDL and non-HDL targets in patients with primary prevention? What's the evidence for using non-HDL, LDL targets in secondary prevention? Then the third one was to look at all lipid lowering medicines and try to adjudicate what's the benefit versus toxicity or risk in patients to reduce cardiovascular events. That covers a pretty broad swatch. So, there are several areas that weren't answered by those questions. Again, the clinical trials weren't necessarily designed to answer clinical questions. Some of them were to have a competitive advantage of one agent over another or to get FDA approval for a particular product and that's an issue.

But I noticed in that brief summary that was released in Orlando, that NLA document, there are clear-cut lipid targets. So, my question is how does that segue with starting a statin ____ (8.27)? Do you anticipate that the NLA recommendations should be used when people have started with the AHA/ACC recommendations and then the numbers just aren't adequate? How should they interface? How would you say the two documents should be used together by the practicing doctor?

Kevin Maki:
Well, in some ways they do outline different approaches. The NLA recommendations are more similar to those of the National Cholesterol Education Program's ATP3 recommendations. So that was kind of the starting point. Then there were modifications made based on additional evidence that was accumulated since those were initially released in 2001. So, the approach and the underlying philosophy is more similar to ATP3 than the approach and philosophy taken by ACC/AHA. So, I think that there is enough overlap that in most cases the initial approach, which will be lifestyle and for those with sufficient risk, statin therapy in probably 80 or 90 percent of the cases you're going to end up in the same place. Now, there are some places where there are differences. One of the differences relates to those individuals who have relatively low levels of atherogenic lipid proteins but have other risk factors, particularly age and hypertension that might put them over the 7.5 percent risk threshold. So, the NLA recommendations in those instances may be less likely to recommend consideration of statin therapy in those with risks between 7.5 and 15 percent.

So, there are some differences and there may end up being some patients for whom there would be less likelihood of starting statin therapy, but in the large majority of cases I think you would end up in a similar place with either approach.

The other place where there are differences is treating to particular goal levels. This is really based on extrapolation from clinical trial data and observational data that align and suggest really that lower is better. But that's a judgment. You can't make that judgment strictly from the clinical trial evidence because the clinical trials didn't treat people to particular targets. So, the expert panel from the NLA was willing to go beyond what the clinical trials have showed and take the approach that lower is better with threshold levels that are related to the level of risk so non-HDL and LDL cholesterol goals for primary prevention, which would be for primary prevention less than 130 and less than 100 for non-HDL and LDL cholesterol. And for secondary prevention, which includes patients with diabetes with two or more risk factors or end organ damage, an LDL cholesterol no less than 70 and an non-HDL cholesterol no less than 100. I should point out all of those are without regard to triglyceride level.

Alan Brown:
So it's very interesting. I've had a little experience with simple messages that's done in our electronic record, putting an alert to start a statin ____ (11.33) going back 15 years in patients who, at that time, had an LDL over 100. Or who had established coronary disease? What we found with that alert on the record was most of the docs started a moderate dose statin, usually Atorva 20 or 40. At the time, the baseline review of the charts and the average doctor there were about 22 percent ____ (11.52) and after that simple message, start a statin ____ (11.55) somewhere upwards of 70 percent were at goal and a huge number of patients over a year, which was encouraging and discouraging as a lipid clinic director.

I went back to look at those people that had high triglycerides to try and find out how many of them were not their non-HDL goal because I was convinced that that would have been missed. It turned out about 89 percent were also at their non-HDL target. So,

I'm running this by you. It strikes me that having that simple message, identify the groups that would benefit from statins starting at moderate or high dose, that probably somewhere in the range of 70 to 80 percent of people, maybe even more at those dosages will achieve their LDL targets that the NLA is recommending. Somewhere around 10 percent will not get their non-HDL. So even the ones that had high triglycerides probably somewhere, roughly 90 percent will get to their non-HDL target by that relatively simple approach. What's left out is what to do with those 10 percent. When we're talking about coronary patients, that's a large number of patients. So my assessment of the beauty of what you're all working on is it gives us some guidance in what to do with those 10 percent and at least take a look at the numbers at the end of the day and decide is there residual risk. Then it's all clinical judgment, as you say, because there aren't the trials. Do you guys have a strategy for using it as a supplement and any recommendation? Should we just look at the NLA recommendations or should we start with the simplified approach that the ACC/AHA recommends?

Kevin Maki:
As I said, I think you can start with either one. In most cases, you'll end up in the same place. I think where the NLA recommendations may have some additional value is in those patients where we don't have good clinical trial data to guide what to do. Also, one of the challenges with use of quantitative risk scoring has been relatively little uptake in clinical practice. So I give talks to physicians and I ask people to raise their hands, how many of you routinely calculate a quantitative risk score. And for every 100 physicians maybe I'll get three or four hands that go up.

Now, in this era of electronic medical records that may start to become more practical. But the reality is most physicians seem to be using sort of risk factor counting and mental calculation approximating a person's risk. So, the NLA algorithm is based first on risk factor counting. It does including quantitative risk scoring. But many patients can be categorized on the basis of either very high or high risk conditions, low risk based on risk factor counting and then you can start looking at other things in the middle. So, it is an alternative for those who are not readily accepting of using the quantitative risk scoring methods recommended by ACC/AHA. Although, for those at moderate risk, quantitative risk scoring can be very helpful for differentiating the really moderate risk versus those who could be bumped up into the higher risk category and treated a bit more aggressively.

Alan Brown:
Kevin, I can't thank you enough for joining us on Lipid Lumiations and giving your insights. I think we're all looking forward to reading the document when it gets published. Thanks for giving us the background of the thought that has gone into it and where it'll fit in with the current published guidelines. I really appreciate it.

Kevin Maki:
Thank you for having me.

Alan Brown:
I'm your host, Dr. Alan Brown. You've been listening today to Lipid Luminations sponsored by the National Lipid Association at ReachMD. If you missed any part of this discussion I would encourage you to visit us at ReachMD.com/lipids to download this podcast and others in the series. Thank you very much for listening and thanks for joining us here in Indianapolis at the National Lipid Association meeting.