Discussion to: Intraoperative ticagrelor removal via hemoadsorption during on-pump coronary artery bypass grafting

Presenter: Michael Schmoeckel, MD
Invited Discussant: Mario Gaudino, MD, PhD
Corresponding Author: Kambiz Hassan, MD

Presenter: Dr Michael Schmoeckel

Dr Mario Gaudino (New York, NY). Thank you for the invitation to discuss this paper. And operating on patients on dual antiplatelet therapy is definitely something we don’t like to do, so your data are important. I disagree with your conclusion, however. You haven’t really shown that your system is effective in reducing ticagrelor dosage. And the reason why you haven’t shown that is because you lack a control group. So, you don’t know what happens in the patients who are in the same exact situation and then undergo bypass surgery without your filter and what would be the ticagrelor level at the end. You have shown what happens in patients who are on ticagrelor who undergo CABG surgery using your device, but we don’t know what happens without your device. That’s a methodological comment that, however, is relevant. And I would disagree with the first statement of your conclusion slide.

My second—well, this is not really a question, it’s a comment. But the question for you—I have 2 questions for you. The first is, what else does this filter eliminate? Okay, ticagrelor is fine, but ticagrelor is not the only molecule that is absorbed. What about, for example, cytokine-activated platelet of neutrophil? Is it possible that there is an additional benefit apart from ticagrelor use? The reason why I asked you that is for my third comment, that I’m not 100% sure that we really need this. Because I know the Swedish data, but there are a lot of other observational data that in fact suggest that even in those very few patients—you have 11 patients in 3 centers, so this is not a very common scenario—but even in those patients that you have to operate within 24 hours after ticagrelor administration, you can do it pretty safely.

There is an increase in moderately severe bleeding events, but generally speaking, there are no important clinical concerns. So, I’m not necessarily sure that the use of this device will lead to clinical benefit. And because of the added cost, I think that will be an important consideration. I’m glad you are testing this in a randomized trial, but I think this is really the missing part of your presentation. Thank you very much.

Dr Michael Schmoeckel (Hamburg, Germany). Thank you very much, Dr Gaudino. Obviously, I agree with your comment that we need this randomized trial, where we have mock absorbers in the circulation, so the surgeon actually doesn’t know whether it’s an active absorber or is just a mock absorber. And then we can tell you whether it’s really effective or not because we have the control group in this randomized trial. This was just a pilot trial to prove that the effect we have seen with the reduced drainage volume, which we compared to a historical group before we used the device—we just took the 2 years before, and we compared those data with the pilot trial in Hamburg. And we just wanted to know is it really a reduction of the ticagrelor or maybe another effect? And you just mentioned that the absorber also takes out other cytokines, and there has been a big study in sepsis patients. Unfortunately, it couldn’t show any benefit, actually, in these patients. Obviously, it takes out some cytokines. But they take out good cytokines and maybe bad cytokines at the same level, and you really don’t know what you’re doing there. And it also takes out, actually, some other drugs, for example, vancomycin. If you use this drug in endocarditis patients, you have to make sure that your vancomycin levels are high enough, and you maybe have to increase the dosage to support your patients with that.
So, I fully agree, this is still a black box. And we need this randomized trial to get the real data, and it’s just a preliminary presentation. And obviously, I am actually quite positive that it will turn out that it’s helpful because I was so convinced after the pilot study we did in Hamburg that I wouldn’t like to do a randomized trial with a mock circulation because, in the middle of the night, I don’t want to stand there with a lot of bleeding and a lot of problems. Just to mention the device price, it’s actually a lot cheaper than the antidotes that you can get for rivaroxaban or apixaban. And for ticagrelor, I think at the moment it’s in a phase 3 trial, the antibody against ticagrelor. So, it’s not really on the market, and there is no alternative for that.

Unidentified Speaker 1. Let’s try to get a couple more quick questions in.

Dr Schmoeckel. Sorry [crosstalk].

Dr Bobby Yanagawa (Toronto, Canada). Just a quick comment. Bobby Yanagawa from Toronto. Thank you. We’re actually involved in this trial. So, it’s been very effective. But prior to this, we used bentracimab, which is the antibody that you mentioned, and we’d just hang it up. A patient that got a bolus of ticagrelor the morning or the night before, within 10 minutes of putting the mini bag up, it’s as if they had no ticagrelor whatsoever. It’s incredibly effective. So, it would be just another option, and—

Unidentified Speaker 1. And what’s the cost of that?

Dr Schmoeckel. Actually, may I just comment that it may be an option, but on the other hand, if you have a patient who had PCI before, and you antagonize it totally, it might be not so beneficial because you may get thrombosis of your stent. And that’s what you don’t want to do.

Dr Yanagawa. Thankfully, we haven’t seen any of those, but time will tell. Thank you.

Unidentified Speaker 1. Doctor Lawton?

Unidentified Speaker 2. I’m delighted that you’re looking at this. I was also curious. I think a greater clinical impact may be if you looked at other dual antiplatelet therapy patients such as prasugrel and clopidogrel, which have a much longer—and the guidelines say 5 to 7 days for those respectively, and ticagrelor is only 3 days. So, they’re really unstable. And ticagrelor—

Dr Schmoeckel. But ticagrelor is reversible. Clopidogrel is irreversible. So, there’s no chance to get rid of it with an absorber. They’re binding to the platelets.

Unidentified Speaker 2. Thank you.

Unidentified Speaker 1. And thank you very much. [applause]