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Reinforcement of Principles, Overcoming Treatment Barriers, and Improving Time to Treatment for ICH

Announcer:
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Dr. Gibler:
So we have this expert group here. It'd be really helpful I think, to Dr. Parry-Jones and his, you know, how he approaches his research to hear from you what you think are the major features that would be helpful? What are the ones that are the greatest barriers for you giving rapid care to these patients with ICH? Is that - you answer that question however you would like to but –

Dr. Parry-Jones:
Yeah, absolutely. I mean, with obtaining a rapid brain imaging, I, you know, as the poll reflects, I think that's usually not a problem for us now, obviously, because we get imaging very quickly to rule out ICH, I guess, so we can give treatments for ischemic stroke. So that's clearly not an issue.

The uncertainty when making the decision to proceed with treatment obviously come up as the second highest. And I presume it's going to be issues relating to when they last took the DOAC, perhaps more than anything, that people are taking time to think about and to decide. The lab results, I think, you know, generally, I would have the view that if there's going to be any significant delay waiting for those, and you're probably best just to get on and treat them. And I guess just switching to that mindset reduces that delay. And as things improve with the laboratory testing in the future, then hopefully we'll be able to minimize the time taken in that step.

Dr. Gibler:
Are the – in your experience, Adrian, or the experience of the audience, are most stroke neurologists, and I would expand that to emergency physicians if they're in the audience, do you have the capability of moving forward without a gatekeeper being a hematologist or someone else within the system determining whether or not you reverse the patient? What is your experience? I guess, a show of hands, do you – are there intermediaries? Are there people that are gatekeepers at your institution that you require a call before you can institute care? Show of hands, how many people have to go through a gatekeeper? So that's very positive. That's good news. With it, and I think that if you look at over the last year or two, that's a tremendous improvement in the situation. By the way, that also reflected the early treatment of acute myocardial infarction with fibrinolytic. And it – and the treatment with acute stroke, ischemic stroke, with fibrinolytic. It gets away from - you know, it gets away from that gatekeeper phenomenon.

Expanding, we have some time. Are there any other questions? I wanted to - we've got a – yeah – yes, please. Yes to the mic, just so everyone can hear your great question.

Male #1:
Well, thank you, Andy, Andrea. I know you as an Andy in Sulphur. So it's a very, very good presentation. It's a very good presentation. And we have taken the guidelines regarding the strict control of the hypertension in ICH, which we're using, but here you indicate that

hypertension is not a factor. Maybe I misunderstood, for the expansion of the, you know, the hematoma.

Dr. Parry-Jones:
Yeah.

Male #1:
The second question is about why edoxaban is not being mentioned on the apixaban and rivaroxaban?

Dr. Parry-Jones:
Okay, so just to take each of those in turn, I think with the blood pressure question, I think there's a lot we don't understand about intensive blood pressure lowering, I think. So if you – what I was referring to there was in the large meta-analysis of predictors of hematoma expansion, high systolic blood pressure at baseline was not an independent predictor of the risk of hematoma expansion, whereas the other things were. So now if you just look specifically at the INTERACT2 trial, which I think probably guides what most of us do, there was not a significant reduction in hematoma expansion in the trial.

Male #1:
Then why do we have so much very restricted by – strictly mentioned monitoring the blood pressure of an ICH, and you're not - we have already, along with your discussion in UK, in our North Region, that ICH and the strict blood pressure of less than 150. And now 150 systolic. So this is the - that is why I raised this question.

Dr. Parry-Jones:
Yeah. So I think the key thing I'm getting at is that so of course INTERACT2 was positive on one of its secondary outcomes with the ordinal shift analysis of that. And we've obviously heard this morning that INTERACT3, the key part of which was blood pressure lowering significantly improves outcome in ICH. So I don't think there's for me, there's no doubt that we should be delivering that to our patients and have been.

But there is a curious disparity between hematoma expansion and outcome in the blood pressure trials. When you put all of them together, which has been done in another big meta-analysis, of trials which gave any intervention to lower blood pressure in the first 7 days, then you do see a reduction hematoma expansion. So I think it's something that always makes me wonder, and I don't think I fully understand it. I don't know if you've got any further comments on it, David, but that's why I put it in there, because I thought it was interesting thing.

Male #1:
Now edoxaban?

Dr. Kreitzer:
Oh, yeah, I was going to get to that question. So we mentioned apixaban and rivaroxaban more frequently in the presentation. And that's just a byproduct of what the label specifically says for andexanet alfa, includes those two anti-Xa's. And the only reason for that is because those are the two agents that were studied in the phase 3 trial. In the phase 4 trial, the ANNEXA-4 study, they allowed all anti-Xa's. So certainly in practice, you could use it for reversal of all anti-Xa's, but the label specifically just includes those two agents because those were the two that were used in a phase 3 study. That's all.

Dr. Seiffge:
I would like to add to the question about hematoma expansion and the blood pressure control issue. I think we have some, at least observational data with situations to suggest that there seems even to be a kind of complementary mechanism if you reverse anticoagulation and you lower blood pressure in patients with anticoagulation ICH. I think it's particularly important in this ICH group on anticoagulants to lower the blood pressure, because these are the patients at highest risk. Although I agree with you that there are - the signals from the study are a bit puzzling, so we don't really understand it from that.

Dr. Parry-Jones:
And it may be that if you treat blood pressure earlier, it does, you know, that, you know, if the window was tighter, that it would have shown a reduction in hematoma expansion and more benefit that. But yeah, I think with the bundle components, there may be more on the sum of their parts as well, and that if you do them all together well, that you get added benefit.

Announcer:
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