Dr Wendler: I believe it has, although I would differentiate between paravalvular leakage and concomitant mitral valve disease. So for the paravalvular leakage I believe it makes a difference if you have a paravalvular leakage or not. And I think it makes sense that the larger the valve you have, the less risky it is maybe to have a paravalvular leakage, because oversizing is easier. However, usually the price you pay for oversizing is that you have increased risk of trauma on the aortic root, and that's the reason why I was quite pleased to see that we don't have more trauma on the aortic root although we have less paravalvular leakage, which is, of course, something quite promising from my point of view.

There is one other thing one needs to keep in mind, and I don't know how much of an impact that has. But these patients are usually treated with a balloon valvuloplasty done with the same size of balloon that you use for the 23 and 26 mm valves. So you could come from a point of view and say that if you have a bigger difference between the diameter of the balloon you use in predilatation and the prosthesis you implant, that may be something which predicts lower risk of paravalvular leakage. The reason could be that you don't predilate the native valve as much, and therefore the valve is pushed tighter into the structure of the native aortic valve. But no one knows that at the moment, but that's one of the explanations I personally have for this.

On the other hand, you mentioned the pacemaker rate. The pacemaker rate is higher, AV block is only 53%, but nevertheless, I personally believed the pacemaker rate is maybe higher because the valve is bigger, and that's the reason why there is maybe more of a risk that you affect the His bundle. On the other hand, from the PREVAIL TA trial we know that there is no difference in incidence of pacemakers between 23, 26, 29. But these are small numbers of patients and therefore I believe that the trial is not necessarily powered for that kind of analysis.

The other question is mitral regurgitation. I think there is a lot of discussion about it. From my point of view, there are only two questions to be answered in this context: first, which patients can you accept for TAVI treatment, so what degree of mitral regurgitation can you accept, and how much will it improve afterwards and, second, what kind of morphology on the mitral valve can you accept? In general, I would say I would not accept too much of a mitral valve disease, because if you treat the aortic valve, usually the mitral valve is not getting much better, and we can see that in around half of the patients. But there are no good data available at present. If you have a patient with functional MR, that is, of course, a different story than if you have another kind of reason why the patient is suffering from MR. So I think there are a lot of questions open, and they have not been answered so far.

Dr V. Falk (Zurich, Switzerland): For transcatheter valves only a limited range of sizes is available, and the 3 mm increments in diameter are bigger than the 2 mm increments for standard biological valves. There are still problems with paravalvular leakage and AV block that can be related to some extent to inappropriate sizing. What is the rationale for not offering a larger variety of valve sizes?

Dr Wendler: Well, to be provocative, I would say one rationale is maybe it is more difficult to produce six different sizes of valves than three different sizes, but that's something which is, of course, a reason which may affect the industry in producing 10 valves of one sort or three valves of one sort. On the other hand, I think one has to be realistic. I mean, in general and in theory I agree with you that it should make a difference if you have more valve sizes. But I think our problem is at the moment maybe not that we don't have enough valve sizes. I think our problem is that we are not good enough at assessing the aortic annulus properly. We don't have a gold standard for how you assess the size of the aortic annulus and how you then make the decision about the size of the valve, because it is not only a decision based on the aortic annulus, but it is a decision based on what size is the left ventricular outflow tract, what size is the aortic root, do you have calcification in the aortic root, how calcified is the aortic valve? I mean, I can tell you that the range for the 29 mm is, for example, 24 to 27, but I have implanted 29 mm valves in an annulus of 30 mm. Why? Because the valve was heavily calcified and therefore there was enough material to protect the valve afterwards and the patient had no paravalvular leakage.

So I think the problem is that we don't have a really good gold standard and a really good way to assess the aortic root and the size in a way that is easily reproducible for everyone. That is the reason why I think it may not matter too much that we don't have the various sizes. But I think it would not be a disadvantage from my point of view.
Third, and perhaps most important, there is a remarkably low rate of paravalvular leak. Specifically, there were only two patients (2.2%) who had a moderate paravalvular leak and 12.8% with mild aortic regurgitation. This contrasts with a 12.2% incidence of moderate or severe paravalvular leak in the Partner cohort A series in which only 23 or 26 mm valves were available [3]. As annular sizing becomes more sophisticated with the realization that echocardiographic assessment frequently undersizes the aortic annulus and that calculation of true aortic annular size by computed tomography scan leads to greater use of larger diameter valves, it could be anticipated that a significant number of patients currently receiving 26-mm valves may in fact be better treated with 29-mm valves and perhaps have less paravalvular leak and thus improved long-term survival.

Fourth, a slight note of caution is warranted, to indicate that there may be a higher permanent pacemaker implantation rate with the 29-mm valve. The pacemaker implantation rate of 12.5% in this series is higher compared with an average 5% pacemaker implantation rate with the 23- and 26-mm Edwards SAPIEN valves. Although this series is small and no conclusions can be definitively drawn, it is possible that the larger valves cause more compression of the membranous septum and therefore a higher permanent pacemaker rate. A larger experience is necessary to determine whether this observation is true.

Fifth, despite the use of the larger valves, it is noteworthy that there were minimal procedural complications including no annular disruptions and a stroke rate of 1.7%. This stroke rate is among the lowest reported with TAVR.

Lastly, it is also quite encouraging that there was no patient prosthesis mismatch and that the effective orifice area (mean 2.5 cm² at 30 days) is higher and the mean aortic transvalvular gradient (8.3 mmHg) is lower than seen with either surgical AVR or the 23- and 26-mm Edwards SAPIEN valves.

From these results, it is readily apparent that the larger-sized 29-mm Edwards SAPIEN XT valve is a valuable addition to the therapeutic armamentarium in treating patients with severe aortic stenosis. As the field continues to grow and assessments of true annular size and patterns of calcification continue to become more sophisticated it will be interesting to observe how much more of a role this additional valve size plays. It has become apparent now in the longer-term follow-up in the multiple series including the 2-year results of the Partner A Trial that even a mild paravalvular leak is associated with an increased long-term mortality [3]. The addition of the larger valve should contribute significantly to the ability to decrease the post-procedure paravalvular leak and thus hopefully improve long-term survival. It will also be interesting to see if more sizes, both larger and smaller, would be helpful.

We are now experiencing currently the maturing of a disruptive technology. As with the experience with the introduction of any new technology into any field, medicine or otherwise, the true value of a disruptive technology comes from the incremental improvements that occur after the initial introduction. In the decade since TAVR was first performed in man, there have been a myriad of incremental improvements in not only the technology but also the implanting techniques, patient selection and post-procedure care. The new, larger-sized valve is yet another example of an incremental improvement that increases and enhances the value of the original technology of TAVR.

**Conflict of interest:** Michael Mack is an uncompensated member of the Executive Committee of the Partner Trial sponsored by Edwards Lifesciences.

**REFERENCES**

