radcliffe cardiology

Title: 5Y Outcomes From the PARTNER 3 Low-Risk Trial
Participants: Dr Martin B Leon
Date: 22/10/23

Dr Martin B Leon

"It's a pleasure to join you. My name is Dr. Martin B. Leon. I'm a professor of cardiology at Columbia University and the Cardiovascular Research Foundation in New York City, and I've been a structural interventionalist and a clinical trialist for most of my career.

Unmet Needs in TAVR Patients in 2023

TAVR has been remarkably successful, with almost 100 procedures being performed in the US this year alone. But there are still some unmet needs.

One of the important unmet needs is that we are continuing to treat lower and lower-risk patients that tend to be younger in age. And in the lower-risk, younger age patients, we expect that their lifespans are longer. So valve durability, which means long term outcomes, becomes an important consideration. That is a major unmet need.

Another unmet need is the treatment of bicuspid aortic valve disease, which also occurs more frequently in younger patients. And a third is the management of redo TAVR in those patients with bioprosthetic valve failure.

The SAPIEN 3 Valve and its Features

Well, the Sapien Three valve has been available for quite some time. It's gone through some minor iterations. The one used in this study was the original Sapien Three valve. So it's been used for more than seven years now. And this is a balloon-expandable valve with a cobalt alloy frame with a bovine pericardial tissue, a trileaflet valve that is intra-annular, relatively short frame balloon expandable and compatible in four sizes with a 14 French expandable sheath delivery system. It also has an external coating which significantly reduces paravalvular regurgitation.

Patient Population and Study Design

The PARTNER Three trial was really the continuation of the fourth series of partner trials, starting from extreme risk to high risk to intermediate risk and now to low-risk patients. The original one-year primary endpoint was reported in 2019 and we're now reporting the five year prespecified endpoint recognising that this study will continue until at least ten years.

The study population were 1000 low-risk, severe symptomatic aortic stenosis patients with a mean age of between 73 and 74 with an STS score of 1.9, much less in the way of severe symptoms. Only 25% to 30% were functional class 304, much less in the way of comorbidities. It was equally divided and randomised one to one between surgical treatment with bioprosthetic valves and transphemeral Sapien Three treatment with TAVR.

Main Findings

Well, the main findings were again, I want to emphasise the follow-up findings because the importance of this was the follow-up over the course of five years and this was recently published, a coincidence with the presentation two weeks ago in the New England Journal of Medicine. So the full manuscript and the supplement are in the New England Journal of Medicine. It is the 8th New England Journal of Medicine publication from the partner series.

The main findings were the primary endpoint, which was a triple composite endpoint of all-cause death, all strokes and rehospitalization for cardiovascular reasons over the course of five years still showed that there was a very strong performance of both TAVR and surgery. A Delta favouring TAVR, which was 7.1% at one year and at that point was statistically significant, which narrowed somewhat to a difference of 4.3%. Still favouring TAVR but no longer statistically significant, the p-value being 0.7. So significant results which indicate that the two technologies are quite similar for this important triple composite endpoint out to five years.

Conclusions

I think the other points in this study which are really meaningful are that we looked at all of the other many endpoints, including the echocardiographic findings. We found that the dramatic improvement in antigrade hemodynamics was sustained over the course of five years, with an overall valve area of 1.87 in the TAVR arm and 1.83 in the surgical arm. Quite similar.

We found, using a quantitative measure of bioprosthetic valve failure, which is a new VARC three definition, that the event rate for valve failure was extremely low, 3.8% in the surgical arm and 3.3% in the TAVR arm, which was less than what we had expected. And that structural valve deterioration, which is a sign of durability, again using very rigorous definitions in a core echo lab, was also extremely low and similar.

And finally, the quality of life for these patients was dramatically improved. They started with a baseline KCCQ score of 70, which increased by about 15 points and then remained stable for five years and was very similar between surgery and TAVR.

So we can tell our patients who are symptomatic, have severe aortic stenosis and are low risk, that at the end of five years they have more than a 70% chance of being alive and having none or very minor symptoms and more than an 85% chance of being alive and having a durable, well-functioning valve. And those are very important findings and we believe show the equivalence of TAVR and surgery, at least for the five year period in a study design like ours.

Further Study Needed

Obviously the study never ends and five years is a very good midpoint to assess valve durability, but we need to carry this out to ten years.

So the ten-year study point is very important. So we'll continue following these patients out to ten years. As I mentioned earlier, the majority of these patients, the mean age was 73. But many patients with aortic stenosis are younger and we have not studied a

younger population. So treating younger patients would also be an important need for the future. And if we can continue to demonstrate good durability, then I would argue that all of the new studies that are being developed that involve preemptive earlier treatment with TAVR either in severe asymptomatic, as or at risk moderate as, become extremely important th and those studies are ongoing, some of which will be reported in the next year or two.