Trials, Triumphs, and Tribulations

The ballroom in our nation’s capitol was packed with thousands expectantly awaiting the presentation of the results. Never has a march on Washington energized so many . . . (interventional cardiologists). Was it a political party, a tea party, or just a party? It was indeed a party to celebrate the results of the PARTNER trial. There were no gasps of disbelief or shocked expressions of surprise, but a quiet recognition that a new era in medicine was dawning. A positive trial was anticipated, and the magnitude of the win did not disappoint.

The Transcatheter Cardiovascular Therapeutics (TCT) meeting has become famous for big production numbers, but the lead-in to this late-breaking trial would have put Broadway to shame. A parade of surgeons and cardiologists who have distinguished themselves as “gurus” of valvular heart disease talked of the challenge of end-stage aortic stenosis using all currently available therapies. A patient just short of her 100th birthday testified to the vigorous new life she had gained from the valve of a stallion, which had saved both her life and the quality of her life. (I thought it was a bovine valve but she was just happy it was not from a pig.) I must admit that she looked so good that in another era she could have sold a lot of “Dr. Smith’s Miracle Youth Elixir.” Finally, with the IMAX and surround sound environment of the Washington Convention Center ballroom in full display, Dr. Marty Leon reported for the investigators the results of the PARTNER trial group B. It was a monumental undertaking, and the investigators deserve enormous credit for the quality of the study.

As we know by now, these were the sickest of the sick. They were aortic stenosis patients, average age 83 years, who were turned down for surgery by some of the country’s best surgeons. It is hard to find a group of patients with any disease who have a 50% 1-year mortality, but this was the fate of the patients who were randomized to medical therapy only. That therapy pulled out all the stops, including aortic valvuloplasty performed in 83% of the control group, but still one-half died by 1 year. Insertion of percutaneous aortic valves, on the other hand, resulted in 70% of patients alive and mostly well at 1 year. There is no question that those who made the pilgrimage to Washington were rewarded with the knowledge that they could tell their grandchildren they were there when it was established that there is no such thing as an untreatable patient with terminal aortic stenosis.

But why was surprise missing? Were there leaks of the data? Surely we now know the penalty for that! No, the results of the trial were tightly held even from the investigators. Yet, why was no one shocked? There was only one reason that this trial would not have been positive. The valve would be a dud! The valve, as futuristic as it may have seemed 2 to 3 years ago, is not viewed as a pipe dream but as a reality. Our European colleagues, unaccustomed to Food and Drug Administration (FDA) regulations, have implanted over 20,000 aortic valves with results that convinced them that the valves were not duds. So, will the impact of the trial live up to the accolades given to it by my colleague, Peter Block (one of the authors of the report) who told me on a CVN interview, “This is the best interventional cardiology trial in a decade.” Is it? Let’s have a look. Certainly this is a very positive trial. An almost halving of mortality is not to be sneezed at, and is unheard of in interventional cardiology trials famous for utilizing component surrogate end points to achieve statistical power.

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available for investigation and therapy exceed most of our expectations, and we hope that excitement will extend beyond the short follow-up we have at present, but 5 to 10 years from now we may view these devices as primitive.

Whether the use of these valves in a broader group of patients will be competitive with surgical repair will be tested in the PARTNER group A study, and this was not established at the time of writing this page. However, their use in the no-option patients studied in PARTNER group B poses some interesting regulatory and ethical issues. Are more trials needed, or would further randomization just be tribulation for the physicians and patients with no options save hospice and valve implantation? Incremental improvements in valves will appropriately require FDA oversight, but will that prevent the use of such devices in patients with no other option? Bram Zuckerman of the FDA, after praising the trial and the investigators, pointed out that the responsibility of the FDA is to analyze the trial and other evidence. He pointed to the variably controlled use outside the U.S., the short-term follow-up, and the complex engineering required to consistently provide a safe and durable product as reasons that careful evaluation is needed. Dangerous or futile therapies have no place in medical practice even for desperate and end-stage situations, but is the current evidence adequate for the use of these devices in appropriately risk-stratified patients who have no other option? The PARTNER group B trial may live up to its spectacular debut as a game changer for the sickest of the sick. For others, we will have to wait on further evidence, including group A results.

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