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CLINICAL INSIGHTS

PORTICO™ TRANSCATHETER AORTIC VALVE IMPLANTATION SYSTEM

Portico™ Valve Meets Non-Inferiority Criteria for Safety and Efficacy in Two-Year Analysis[1]

No significant difference in mortality or disabling stroke between groups

PUBLICATION TITLE

Self-expanding intra-annular versus commercially available transcatheter heart valves in high and extreme risk patients with severe aortic stenosis (PORTICO IDE): a randomised, controlled, non-inferiority trial

AUTHORS

Raj R. Makkar, Wen Cheng, Ron Waksman, et al.

METHODS

- Prospective, multicenter, non-inferiority, randomized controlled trial
- 750 High- and extreme-risk patients with severe symptomatic aortic stenosis enrolled from 52 sites in the US and Australia

Participants randomized to undergo transcatheter aortic valve replacement with either:

- Portico™ valve and first-generation delivery system, or
- Any FDA approved and commercially available valve (CAV): Balloon expandable Edwards-SAPIEN‡, SAPIEN XT‡, or SAPIEN‡ 3; or supra-annular self-expanding CoreValve‡, Evolut-R‡, or Evolut-PRO‡.

CAV selection was at investigator discretion and allowed use of the latest FDA-approved model, which were used in 88% of the control group.

- **Primary safety endpoint**: composite of all-cause mortality, disabling stroke, life-threatening bleeding requiring transfusion, acute kidney injury requiring dialysis, or major vascular complication at 30 days
- **Primary efficacy endpoint**: all-cause mortality or disabling stroke at 1 year

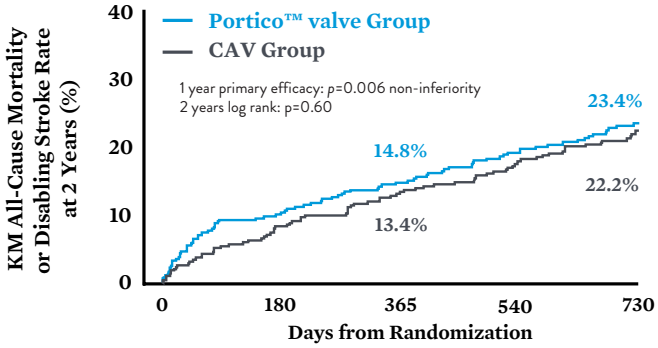
RESULTS

From May 2014 to October 2017, patients were randomized (1:1) to Portico valve (n=381) and CAV (n=369) groups. No differences in all-cause mortality or disabling stroke were found at 1 year or 2 years (see Figure 1).

- Portico valve met the non-inferiority criteria for the primary safety endpoint in the intention-to-treat (ITT) population, 13.8% (Portico valve) and 9.6% (CAV); $p_{\text{non-inferiority}}$=0.034; but not in the as-treated population $p_{\text{non-inferiority}}$=0.071.
- Primary efficacy endpoint rates were similar between the Portico valve (14.8%) and CAV (13.4%) groups at 1 year; $p_{\text{non-inferiority}}$=0.0058, and met non-inferiority criteria.

Mean aortic valve gradients were lower and mean aortic valve area greater in the Portico valve group than the CAV group at 30 days, 1 year, and 2 years. The self-expanding intra-annular Portico valve's hemodynamic profile was significantly better than balloon-expandable intra-annular valves and comparable to self-expanding supra-annular valves. (see Figure 2).

Figure 1. No difference in all-cause mortality or disabling stroke rate at one year or two years was seen between the groups (ITT population).[2]



Portico valve group	381	330	308	273	223
CAV group	369	330	306	273	231

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POST HOC ANALYSIS

Multiple factors, including concurrent improvements to CAV platforms may have affected the trial and the study described the importance of the learning curve.

- Authors noted disproportionate implant experience with CAV-group devices versus Portico™ valve.
- Median attempted implants with Portico valves was 5 per site. Only 5 sites attempted more than 20 implants.

Primary efficacy endpoint rates improved in the Portico valve group when comparing enrollment from the first half of the trial to the second while the CAV group efficacy event rates remained stable (see Table 1). Specifically, all-cause mortality at 1 year in the Portico valve group decreased from 16.3% in first-half participants to 12.4% for those enrolling later.

- In first half of the trial, major vascular complications drove 30-day safety endpoint rates higher in the Portico valve group than the CAV group (16.0% vs 7.7%, respectively; *p*=0.012).
- Primary safety endpoint rates were not significantly different between groups in second half of trial (11.6% Portico valve group vs 11.5% CAV group)

CONCLUSIONS

Portico valve met the prespecified non-inferiority criteria for the primary safety and efficacy endpoints. The primary safety endpoint at 30 days was met in the ITT population and the trial met the pre-specified primary efficacy endpoint at 1 year in the ITT and as-treated populations. A concurrently published single-arm study of the Portico valve with the FlexNav™ delivery system has reported data of improvements in safety outcomes.[3]

Figure 2. Portico™ valve had (A) similar mean aortic valve gradients and areas to Evolut‡ R and Evolut‡ PRO; and (B) lower aortic valve gradients and larger valve areas than SAPIEN‡ 3 valves through 2 years.

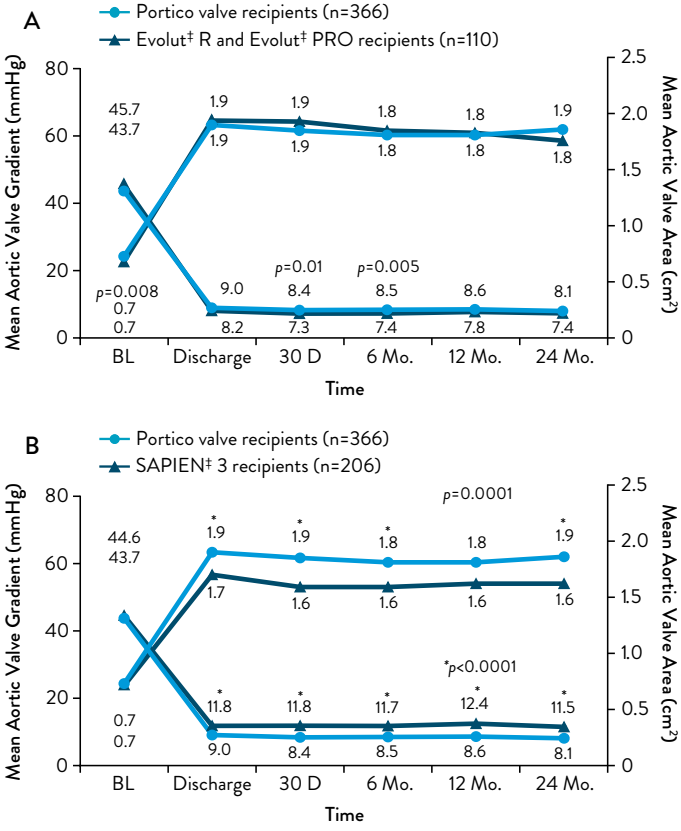

Table 1. ITT Analysis of Primary Endpoints by Enrollment Phase

Enrollment	1st Half*				2nd Half**			
Outcome / Group	Portico™ (n=191)	CAV (n=184)	Dif.	*P*	Portico (n=190)	CAV (n=185)	Dif.	*P*
Primary safety endpoint at 30 days	16.0%	7.7%	8.4%	0.01	11.6%	11.5%	0.1%	0.97
Primary efficacy endpoint at 1 year	17.4%	13.3%	4.0%	0.27	12.4%	13.4%	-1.0%	0.84

Dif. = difference; yr = year. *Day of randomization May 30, 2014, to December 21, 2016. **Day of randomization December 22, 2016, to October 10, 2017.

REFERENCE:

1. Makkar RR, Cheng W, Waksman R, et al. Self-expanding intra-annular versus commercially available transcatheter heart valves in high and extreme risk patients with severe aortic stenosis (PORTICO IDE): a randomised, controlled, non-inferiority trial. *Lancet*. 2020 Sep 5;396(10252):669-683.
2. Makkar RR. Comparison of two-year outcomes for an investigational self-expanding transcatheter aortic valve verses commercially-available valves: Results from the PORTICO IDE trial. Presented at the PCR e-Course, June 26, 2020.
3. Fontana GP, Bedogni F, Groh M, et al. Safety Profile of an Intra-Annular Self-Expanding Transcatheter Aortic Valve and Next-Generation Low-Profile Delivery System. *J Am Coll Cardiol Intv*. 2020;13:2467–78.

Abbott
3200 Lakeside Dr., Santa Clara, CA 95054 USA

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