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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

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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

See Important Safety Information referenced within.

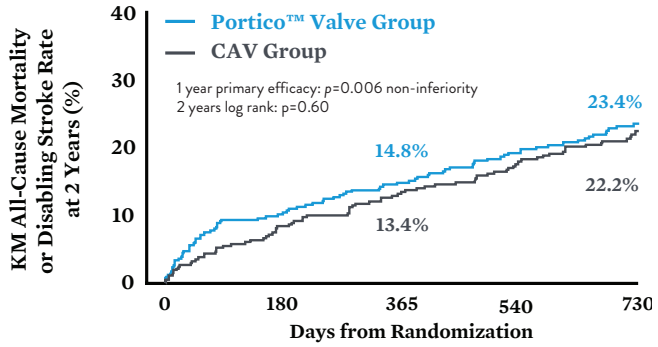
RESULTS

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

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.

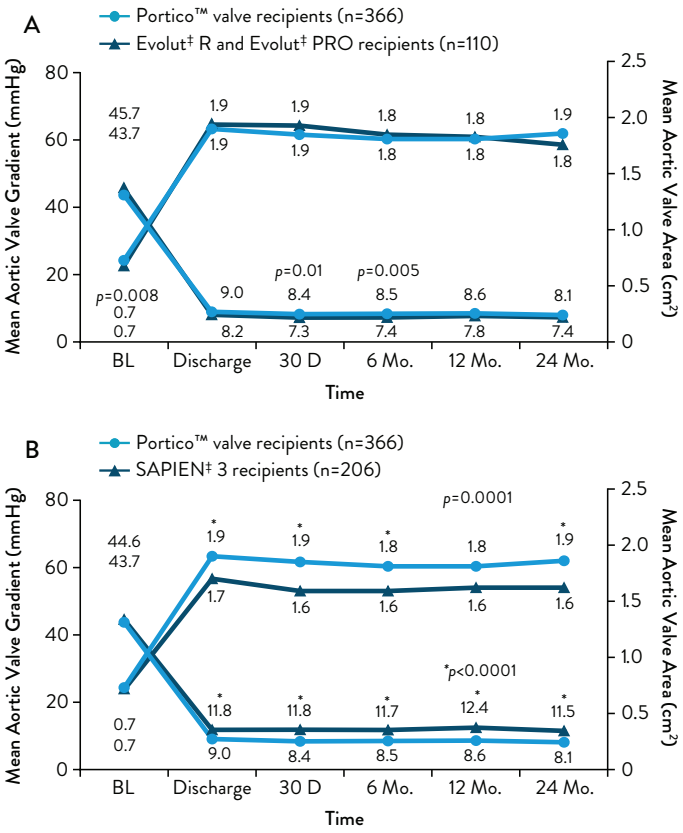


Table 1. ITT Analysis of Primary Endpoints by Enrollment Phase

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.

See Important Safety Information referenced within.

PORTICO™ TRANSCATHETER AORTIC VALVE IMPLANTATION SYSTEM

IMPORTANT SAFETY INFORMATION

Rx ONLY

INDICATIONS

The Portico™ Transcatheter Aortic Valve Implantation System is indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be high or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 8% at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical comorbidities unmeasured by the STS risk calculator).

CONTRAINDICATIONS

The valve is contraindicated for patients with inability to tolerate antiplatelet/anticoagulant therapy or nitinol alloy (nickel and titanium), or who have active infections, including endocarditis.

WARNINGS

Carefully read all warnings, precautions, and instructions for use for all components of the system before use. Failure to read and follow all instructions or failure to observe all stated warnings could cause serious injury or death to the patient.

- Perform Portico™ valve implantation in a facility where emergency aortic valve surgery is available.
- Verify that the patient's anatomy is consistent with the specifications set forth in the anatomical specifications tables 2 and 3 (found in IFU).
- For single use only. Do not reuse, reprocess, or resterilize the valve, delivery system, or the loading system. Reuse, reprocessing, and/or resterilization creates a risk of contamination of the devices and/or device failure, which could cause patient injury, illness or death.
- Do not manipulate or handle the valve with sharp or pointed objects.
- Rinse the valve as directed before loading the valve onto the delivery system.
- Do not use the valve, the delivery system, or the loading system if the "USE BY" date has elapsed.
- Exercise care to prevent kinking of the delivery system when removing it from the packaging.
- This device contains nitinol, an alloy of nickel and titanium. Persons with allergic reactions to these metals may suffer an allergic reaction to this implant. Prior to implantation, patients should be counseled on the materials contained in the device, as well as potential for allergy/ hypersensitivity to these materials.
- Accelerated deterioration of the valve due to calcific degeneration may occur in children, adolescents, young adults, or patients with altered calcium metabolism.

PRECAUTIONS

Pre-Implantation Precautions

- The safety, effectiveness, and durability of a Portico™ valve implanted within a surgical or transcatheter bioprosthesis have not been demonstrated.
- Long-term durability has not been established for the Portico valve. Regular medical follow-up is advised to evaluate valve performance.
- For transaortic access, ensure the access site and trajectory are free of internal patent right internal mammary artery (RIMA) or pre-existing patent RIMA graft.
- For subclavian/axillary access, use caution in patients with mammary artery grafts.
- Balloon aortic valvuloplasty (BAV) of the native aortic valve is recommended prior to delivery system insertion. The balloon size chosen should be appropriate, not exceeding the minimum diameter of the native aortic annulus as assessed by CT imaging to minimize risk of annular rupture and not undersized to minimize risk of stent under-expansion which could lead to paravalvular leak (PVL) or device migration.
- Do not use the valve if the shipping temperature indicator on the product package has turned red, or if the valve has been improperly stored in temperature conditions outside of the 5°C–25°C (41°F–77°F) range.
- Do not use the valve if the tamper-evident container seal is damaged, broken, or missing, or if fluid is leaking from the packaging.
- Do not advance the delivery system without the guidewire extending from the tip.
- Do not use the valve without thoroughly rinsing as directed.
- Do not use the delivery system without thoroughly flushing as described in the "Directions for Use" section.
- The safety and effectiveness of the Portico™ valve and FlexNav™ delivery system have not been evaluated in the following patient populations:
  - Congenital unicuspid or bicuspid valve, or any leaflet configuration other than tricuspid
  - Severe ventricular dysfunction with left ventricular ejection fraction <20%
  - Non-calcific aortic annulus
  - Echocardiographic evidence of intracardiac mass, thrombus or vegetation
  - Patients at low or intermediate surgical risk
  - Patients who are pregnant or breastfeeding
  - Pediatric patients (less than 21 years of age)
  - Patients with a pre-existing prosthetic heart valve or prosthetic ring in any position
  - Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation > 3+)
  - Patients with severe circumferential mitral annular calcification (MAC) which is continuous with calcium in the LVOT, severe (greater than 3+) mitral insufficiency, or severe mitral stenosis with pulmonary compromise
  - Blood dyscrasias as defined: leukopenia (WBC<3000 mm^3), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count <50,000 cells/mm^3)
  - Patients with untreated clinically significant coronary artery disease requiring revascularization
  - Patients with bulky calcified aortic valve leaflets in close proximity to coronary ostia
  - Hypertrophic cardiomyopathy with or without obstruction (HOCM)
  - Renal insufficiency (creatinine > 3.0 mg/dL) and/or end stage renal disease requiring chronic dialysis
  - Hemodynamic instability requiring inotropic support or mechanical heart assistance
  - Significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5cm or greater; marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe "unfolding" and tortuosity of the thoracic aorta
  - Patients with known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media which cannot be adequately premedicated
  - Patients with access characteristics that would preclude safe placement of the introducer sheath, when necessary, such as severe obstructive calcification, or severe tortuosity

Implantation Precautions

- To minimize risk of guidewire perforations in the left ventricle, a manufacturer pre-shaped guidewire should be used during the procedure and during valve deployment.
- Do not deploy the valve if excessive resistance to deployment is encountered. If the valve does not deploy easily, re-sheath the valve, remove it from the patient, and use a different valve and delivery system.
- Follow the procedure in "Implanting the Valve" to reposition the valve or to remove the valve from the patient.
- Do not attempt to reposition the valve by advancing it distally unless the valve has been fully re-sheathed within the delivery system.
- Do not re-sheath the valve more than two times prior to final valve release. Additional re-sheath attempts may compromise product performance.
- To minimize likelihood of permanent pacemaker implantation (PPI): a) maintain implant depth of 3mm, and b) limit manipulations across the LVOT.

Post-Implantation Precautions

- In the event that a post-implant balloon dilatation is performed to address paravalvular leak (PVL), valve size, patient anatomy, and implant depth must be considered when selecting the size of the balloon for dilatation. The balloon size chosen should not exceed the mean diameter of the native aortic annulus. Moderate or Severe PVL should be addressed at the time of the TAVI procedure.
- Exercise care when removing the delivery system from the patient.
- Exercise care when crossing the valve with adjunctive devices.
- Once the valve is fully deployed, repositioning and retrieval of the valve is not possible. Attempted retrieval (e.g., use of a guidewire, snare, or forceps) may cause aortic root, coronary artery, and/or myocardial damage.
- Valve recipients should be maintained on antiplatelet and/or anticoagulant therapy post procedure, per institutional standards and established guidelines, except when contraindicated, using individualized treatment as determined by their physician.
- Post-implant monitoring and/or possible electrophysiology evaluation may be considered in patients with transient high degree or complete AV block or other conduction disturbances during or following implantation of the valve. This may include continuous ECG monitoring after hospital discharge.

POTENTIAL ADVERSE EVENTS

Adverse events potentially associated with the use of transcatheter bioprosthetic heart valves include but are not limited to:

- access site complications (e.g., pain, bleeding, infection, hematoma, pseudoaneurysm, etc.)
- acute coronary obstruction
- acute myocardial infarction
- allergic reaction to antiplatelet agents, contrast medium, or valve components
- aortic rupture
- ascending aorta trauma
- atrio-ventricular node block
- cardiac arrhythmias
- conduction system injury
- conversion to open surgical procedure
- death
- dissection
- embolism
- emergent balloon valvuloplasty
- emergent percutaneous coronary intervention (PCI)
- emergent surgery (i.e., coronary artery bypass, heart valve replacement)
- endocarditis
- explantation
- heart failure
- hemodynamic compromise
- hemolysis
- hemolytic anemia
- hemorrhage
- hypotension or hypertension
- infection
- myocardial ischemia
- mitral valve insufficiency
- multi-organ failure
- non-structural dysfunction (i.e., entrapment by pannus, paravalvular leak, inappropriate sizing or positioning)
- pannus
- pericardial effusion
- perforation of the myocardium, ventricle, or a blood vessel
- permanent disability
- permanent pacemaker
- regurgitation
- renal insufficiency or renal failure
- reoperation
- respiratory failure
- sepsis
- stroke
- structural deterioration (i.e., calcification, leaflet tear)
- thrombosis
- tamponade
- transfusion
- valve embolization or migration
- vessel dissection or spasm

CAUTION: This product is intended for use by or under the direction of a physician. Prior to use, reference the Instructions for Use, inside the product carton (when available) or at eifu.abbottvascular.com or at medical.abbott/manuals for more detailed information on Indications, Contraindications, Warnings, Precautions and Adverse Events.

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