The PARTNER Cohort B randomized 358 inoperable patients with symptoms of severe AS to transfemoral TAVI (n=179) versus standard therapy (n=179). Included patients were NYHA class II or higher and had severe AS (echo valve area of <0.8 cm^2 [EOA index < 0.5 cm^2], mean gradient >40 mm Hg or jet velocity >4.0 m/s) and a >50% risk of death or serious irreversible morbidity with surgical aortic valve replacement as assessed by a cardiologist and two surgeons). The primary endpoint was all-cause mortality over the length of the trial. Other key endpoints were: cardiac mortality, rehospitalization, stroke, NYHA functional class, days alive and out of the hospital, echo-derived valve area, transvalvular gradients, paravalvular aortic regurgitation, and mortality outcomes that were stratified by STS score.

Eleven patients crossed over from standard therapy to TAVI between 1 and 2 years. All-cause mortality (intention to treat; ITT), including crossover patients, was significantly lower at 2 years for patients who were treated with TAVI versus standard therapy (67.6% vs 43.3%, respectively; HR=0.57; 95% CI, 0.44 to 0.75; p<0.0001). Censoring of the crossover patients did not qualitatively change the results.

A landmark analysis was performed among the survivors at 1 year to ascertain whether there was incremental benefit between Years 1 and 2. Among the 1-year survivors, mortality was 18.2% with TAVI versus 35.1% with standard therapy (HR=0.58; 95% CI, 0.37 to 0.92; p=0.019).

Cardiovascular (CV) mortality (ITT, crossover patients censored) was 31.0% with TAVI versus 62.4% with standard therapy (HR=0.44; 95% CI, 0.32 to 0.60; p=0.0001). The rate of repeat hospitalizations (ITT) was 35.0% in the TAVI group versus 72.5% in the standard therapy group (HR=0.41; 95% CI, 0.30 to 0.58; p=0.0001). The days alive out of the hospital was 699 with TAVI versus 355 with standard therapy (p=0.0003). TAVI improved NYHA functional status and decreased Class III/IV symptoms versus standard therapy (17% vs 64%; p<0.001).

There were more neurological events with TAVI versus standard therapy (16.2% vs 5.5%, respectively; p=0.003). The incidence of stroke at 2 years was 13.8% in the TAVI group versus 5.5% in the standard therapy group (HR=2.79; 95% CI, 1.25 to 6.22; p=0.009). After 30 days, differences in stroke frequency were largely due to increased hemorrhagic strokes in TAVI patients.

In patients who were not suitable for surgery, TAVI was superior to standard therapy, with incremental benefit from 1 to 2 years, markedly reducing the rates of all-cause mortality, CV mortality, and repeat hospitalization, with improved NYHA functional status and decreased Class III/IV heart failure symptoms. Importantly, TAVI patients had significantly increased rates of stroke. TAVI was most beneficial in patients without extreme clinical comorbidities.

Dr. Makkar concluded that the 2-year data continue to support the role of TAVI as standard of care for symptomatic patients with AS who are not surgical candidates.

Transapical TAVI Inferior to SAVR in Operable Elderly Patients

Transcatheter aortic valve implantation (TAVI) is a treatment option for patients with aortic valve stenosis who are either high risk or not operative candidates for conventional surgical aortic valve replacement (SAVR). Transfemoral TAVI requires delivery of the valve system through the iliofemoral vasculature and is limited by peripheral vascular disease (PVD) and small vessel caliber. Transapical TAVI is somewhat more invasive than the transfemoral approach but can be utilized in patients with severe PVD or smaller leg vessels. The role of TAVI in patients who are operable candidates or at lower surgical risk has not been studied. Leif Thuesen, MD, Aarhus University Hospital, Aarhus, Denmark, presented the Prospective, Randomized Trial of Transapical Transcatheter Aortic Valve Implantation versus Surgical Aortic Valve Replacement in Operable Elderly Patients with Aortic Stenosis (STACCATO) trial. The objective of STACCATO was to evaluate the safety and efficacy of transapical TAVI in operable, lower-risk patients.

A total of 72 patients were randomized to transapical TAVI (n=34) or SAVR (n=36). Two patients were excluded after randomization. Eligibility criteria included valvular aortic stenosis (valve area <1.0 cm^2), age ≥70 years (later amended to age ≥75 years), patients who were treatable by either transapical TAVI or SAVR, and expected survival >1 year following successful treatment. The primary endpoint was the composite of 30-day all-cause mortality, major stroke, and/or renal failure that required dialysis.

The study design called for inclusion of 200 patients. After inclusion of 11 patients, the study was put on hold due to 3 potentially serious adverse events in the transapical TAVI group. After inclusion and exclusion criteria were modified (increased age limit to 75 years and exclusion for previous heart surgery), the study was resumed.

After randomization of 70 patients, the independent data safety monitoring board recommended study termination

due to an excess number of adverse events in the transapical TAVI group. Primary endpoint events occurred in 5 patients in the transapical TAVI group and 1 patient in the SAVR group within 3 months (p=0.07; Table 1).

Table 1. Primary Endpoint Events.

Allocation	Event	Time of event	Outcome
Transapical TAVI	Death	On waiting list	Not treatment related
Transapical TAVI	Left coronary artery blockage	Perioperative	Acute CABG/ SAVR, death Day 1
Transapical TAVI	Major stroke	Day 27	Severe disability, death Day 34
Transapical TAVI	Major stroke	Day 16	Severe disability
Transapical TAVI	Renal failure requiring dialysis	Day 8	Hemodialysis
SAVR	Major stroke	Perioperative	Severe disability

After treatment, the mean aortic valve area increased from baseline in the transapical TAVI group from 0.66 cm^2 to 1.4 cm^2 (p<0.0001) and in the SAVR group from 0.71 cm^2 to 1.3 cm^2 (p <0.0001). Baseline peak aortic gradient was higher in the transapical TAVI group compared with the SAVR group. Both groups had lower gradients after treatment (p<0.0001), with a lower gradient in the transapical TAVI group than in the SAVR group (p=0.07). Paravalvular leakage after treatment was more frequent with transapical TAVI than SAVR (p<0.001; Table 2). The NYHA class was significantly improved from baseline in both the transapical TAVI (p=0.01) and SAVR (p=0.001) groups.

Table 2. Paravalvular Leakage.

	Transapical TAVI	SAVR	p value
Aortic valve area (cm^2)			
Baseline	0.66	0.71	<0.0001*
After treatment	1.4**	1.3**	
Peak aortic gradient (mm Hg)			
Baseline	80	67	<0.0001*
After treatment	20	24	
Paravalvular leakage after treatment n (%)			
Moderate to severe	4 (13)	0	<0.001†
Minimal	13 (43)	2 (6)	
None	13 (43)	33 (94)	

*change from baseline to after treatment; **estimated from Figure; †difference between groups.

The study was limited by the inclusion of only two enrolling centers with some experience in performing transapical TAVI. Furthermore, preoperative use of multislice CT was not utilized to optimize valve sizing and positioning relative to the left main. Since the trial was terminated early, the estimates of the risks and benefits may be less precise due to a smaller sample size than had been planned.

Prof. Thuesen concluded that in its present phase of development, transapical TAVI appears to be inferior to SAVR in low-risk, operable, elderly patients. This study highlights the importance of patient selection, noninvasive preprocedural assessment, and the current indications for the procedure; TAVI should be used in nonoperable or surgically very high-risk patients. The role of transapical TAVI requires further investigation to determine what clinical role it may have.

Primary Results of ADVISE: Validation of a Vasodilator Independent Measure of Coronary Fractional Flow Reserve

Fractional flow reserve (FFR) is a diagnostic tool that is utilized during coronary angiography to determine the physiological significance of a coronary artery stenosis. FFR is defined as the ratio of the pressure that is distal to a stenosis relative to the pressure before the stenosis during maximal hyperemia. Although FFR has been validated in clinical trials and correlated with improved outcomes, recent evidence has shown that only 6% of percutaneous coronary interventions (PCIs) in the United States are performed with FFR guidance [Kleiman NS et al. *J Am Coll Cardiol* 2011]. A major barrier to its use is the current requirement for vasodilator drugs, such as adenosine, which may be contraindicated or disliked by patients, and it adds to procedural time and costs, inconvenience, and risk [Pijls N. *J Am Coll Cardiol Interv* 2011].

Justin Davies, MD, PhD, Imperial College, London, UK, presented the results of the ADVISE trial, which evaluated instantaneous wave-free ratio (iFR), a new technology that assesses coronary stenosis using pressure as a surrogate for coronary flow during a period of naturally occurring stable resistance, thereby avoiding the need for adenosine or other vasodilators.

The first part (proof-of-concept) of the ADVISE study evaluated resting wave-free resistance versus mean hyperemic resistance in 39 patients. Study assessments included intracoronary pressure and flow velocity measurements, baseline resistance assessment, and resistance assessment under pharmacological