ACC.15
TCT@ACC-i2 | innovation in intervention
64th Annual Scientific Session & Expo

An All-comers Randomized Clinical Trial Comparing Transcatheter with Surgical Aortic Valve Replacement in Patients with Aortic Valve Stenosis

On behalf of NOTION investigators:

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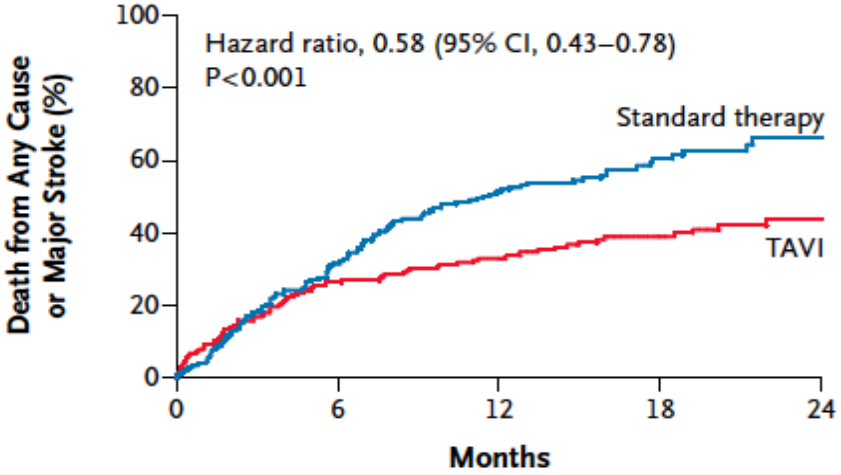
MARCH 14 – 16, 2015
SAN DIEGO
CALIFORNIA

Funding

- The Danish Heart Foundation

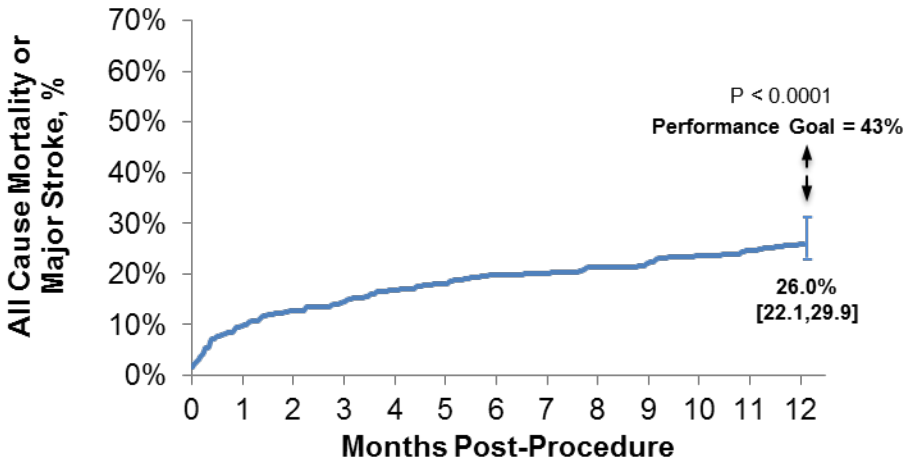
TAVR in Extreme-Risk Patients

PARTNER TRIAL



Leon MB et al, NEJM 2010

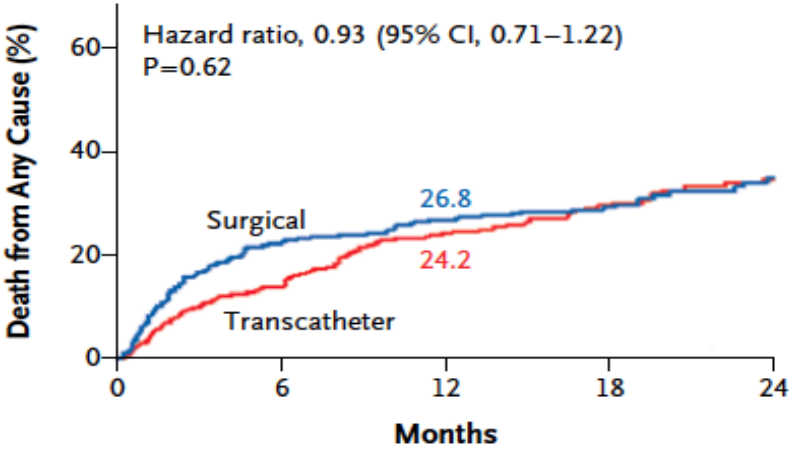
US COREVALVE EXTREME RISK STUDY



Popma JJ et al, JACC 2014

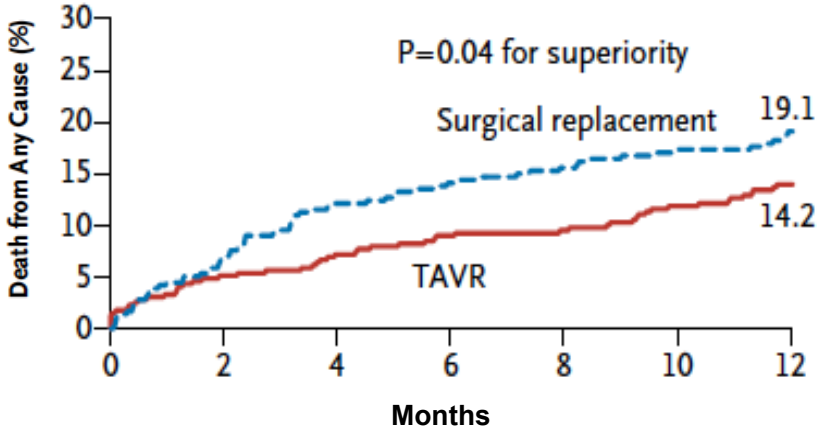
TAVR in High-Risk Patients

PARTNER TRIAL



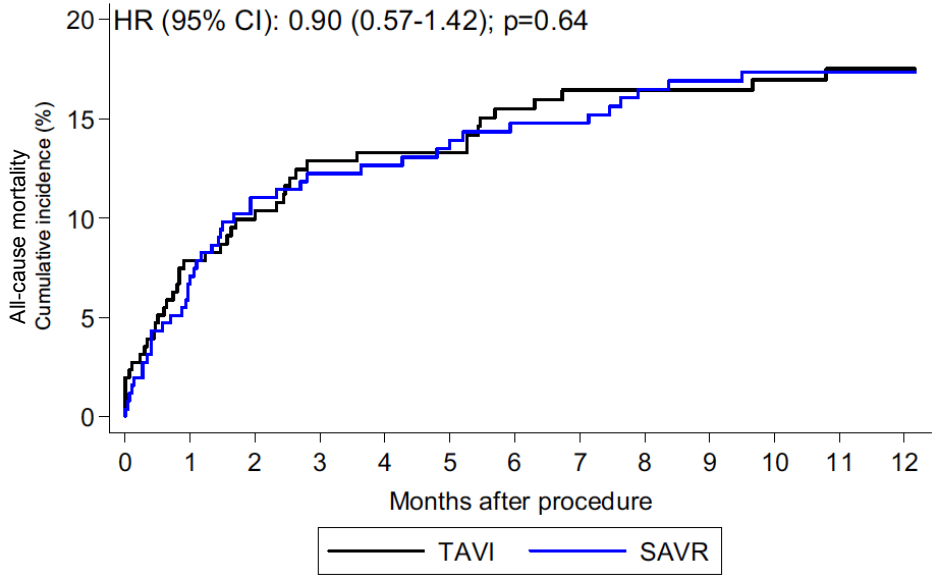
Smith CR et al, NEJM 2011

US COREVALVE HIGH RISK STUDY



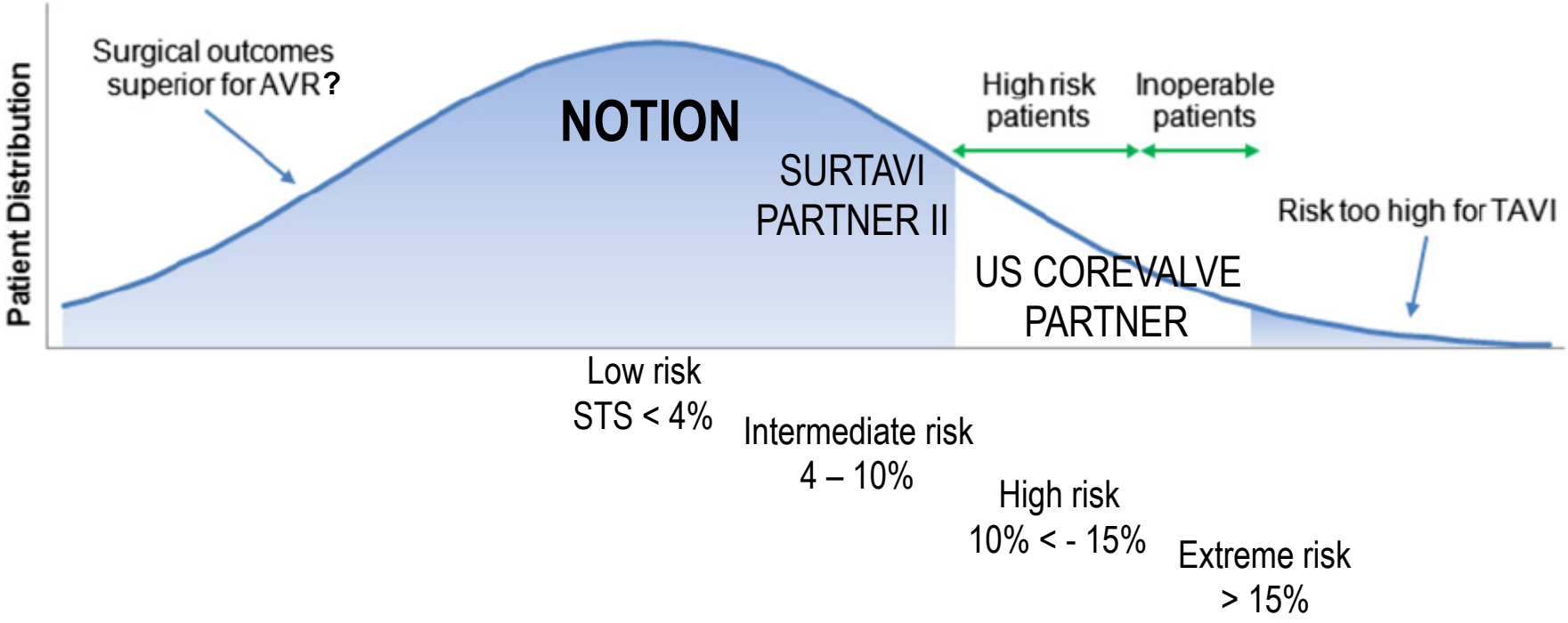
Adams DH et al, NEJM 2014

TAVR in Intermediate-Risk Patients



Propensity-score matched study
Piazza et al, JACC 2014

Operative Risk and TAVR vs. SAVR Trials

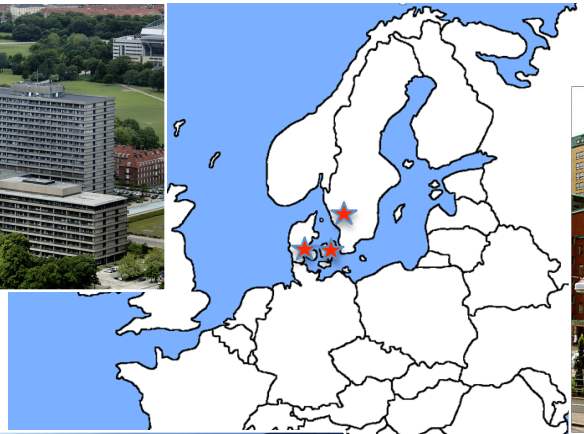


Nordic Aortic Valve Intervention (NOTION) Trial

Objective:	Compare TAVR vs. SAVR in patients ≥ 70 years eligible for surgery (all-comers population)
Primary outcome:	Composite rate of death from any cause, stroke or myocardial infarction at 1 year (VARC II-defined)
Secondary outcomes:	Safety and efficacy (NYHA), echocardiographic outcomes (VARC II-defined)
Design:	Prospective, multicenter, non-blinded, randomized trial
Enrollment period:	December 2009 - April 2013

Participating Centers

Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark



Sahlgrenska University Hospital, Gothenburg, Sweden

Odense University Hospital, Odense, Denmark

Trial Investigators and CEC

Principal Investigators:

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Nikolaj Ihlemann

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Lars Willy Andersen

Henrik Nissen

Bo Juel Kjeldsen

Petur Petursson

Clinical Events Committee:

Kristian Thygesen (chair), cardiologist

Bo Norrving, neurologist

Torben Schroeder, vascular surgeon

Enrollment Criteria

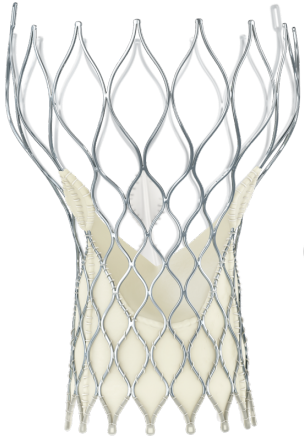
Main inclusion criteria:

- 70 years or older
- Severe aortic valve stenosis on echocardiogram
- Expected to live more than 1 year
- Anatomical suitable for both procedures

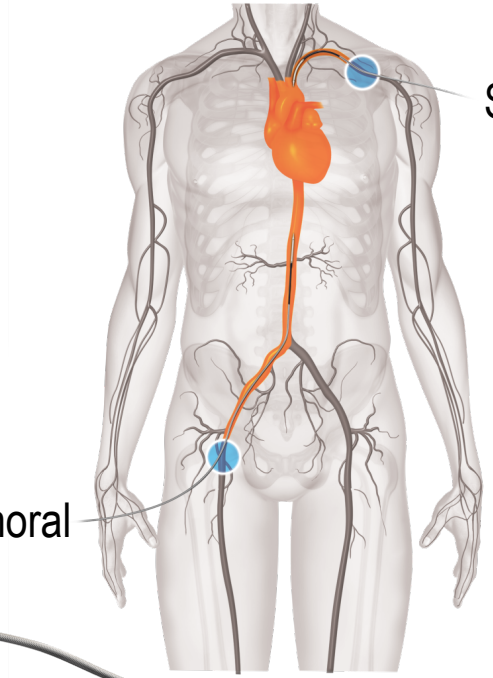
Main exclusion criteria:

- Severe coronary artery disease
- Severe other heart valve disease
- Prior heart surgery
- Indication for acute treatment
- Recent stroke or myocardial infarction
- Severe pulmonary or renal failure

Device and Access Routes



Self-expanding
bio-prosthesis
4 valve sizes
(annulus diameter
18-29 mm)



18 Fr delivery system

Sample Size Determination

Alternative hypothesis: TAVR is superior to SAVR regarding the composite rate of death from any cause, stroke or myocardial infarction after 1 year

Sample Size Determination:

1:1 treatment allocation
Two-sided alpha = 0.05
Power = 80%

Expected $rate_{SAVR}$ = 15%
Expected $rate_{TAVR}$ = 5%

Trial Size: 280 patients

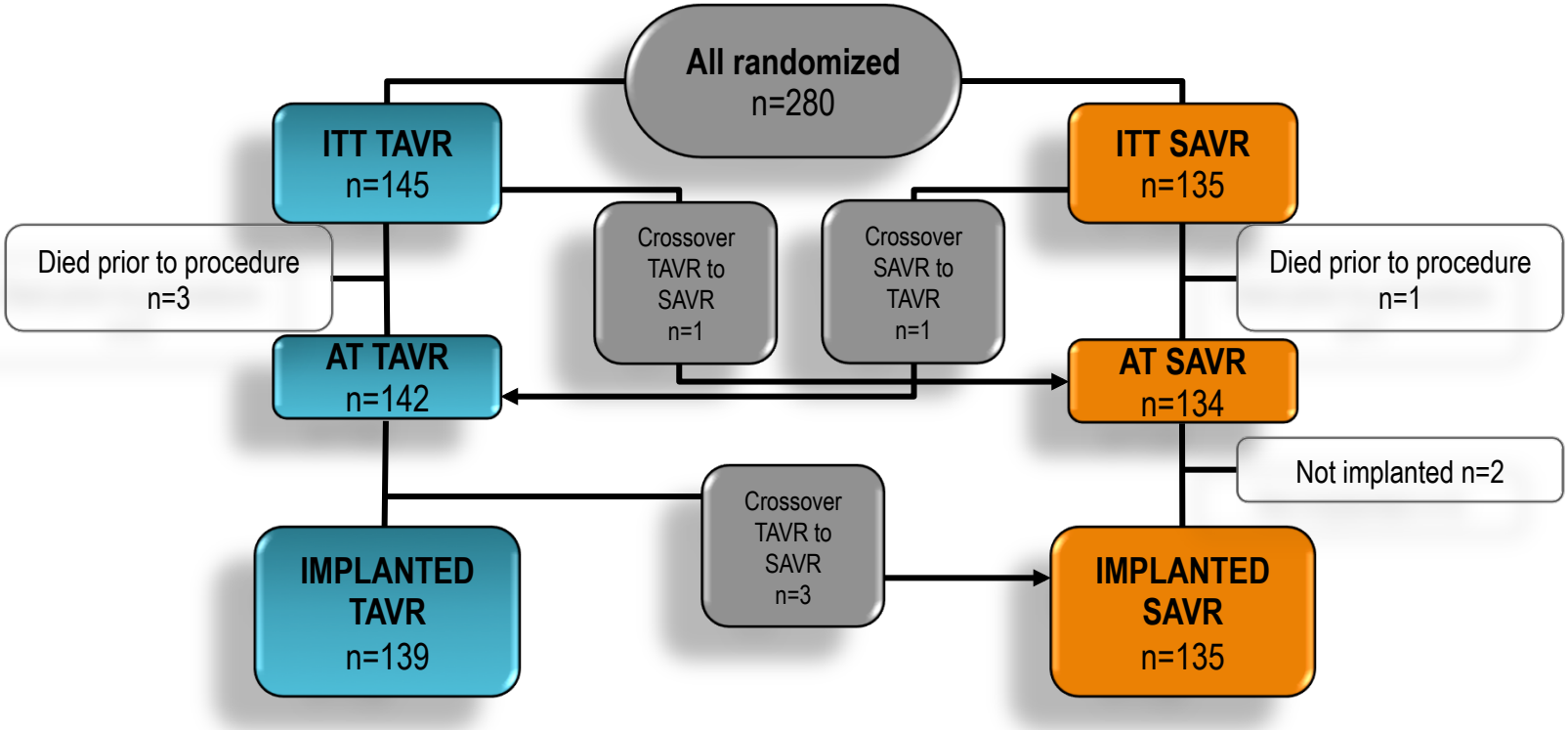
Primary Analysis Population

- Intention-to-treat

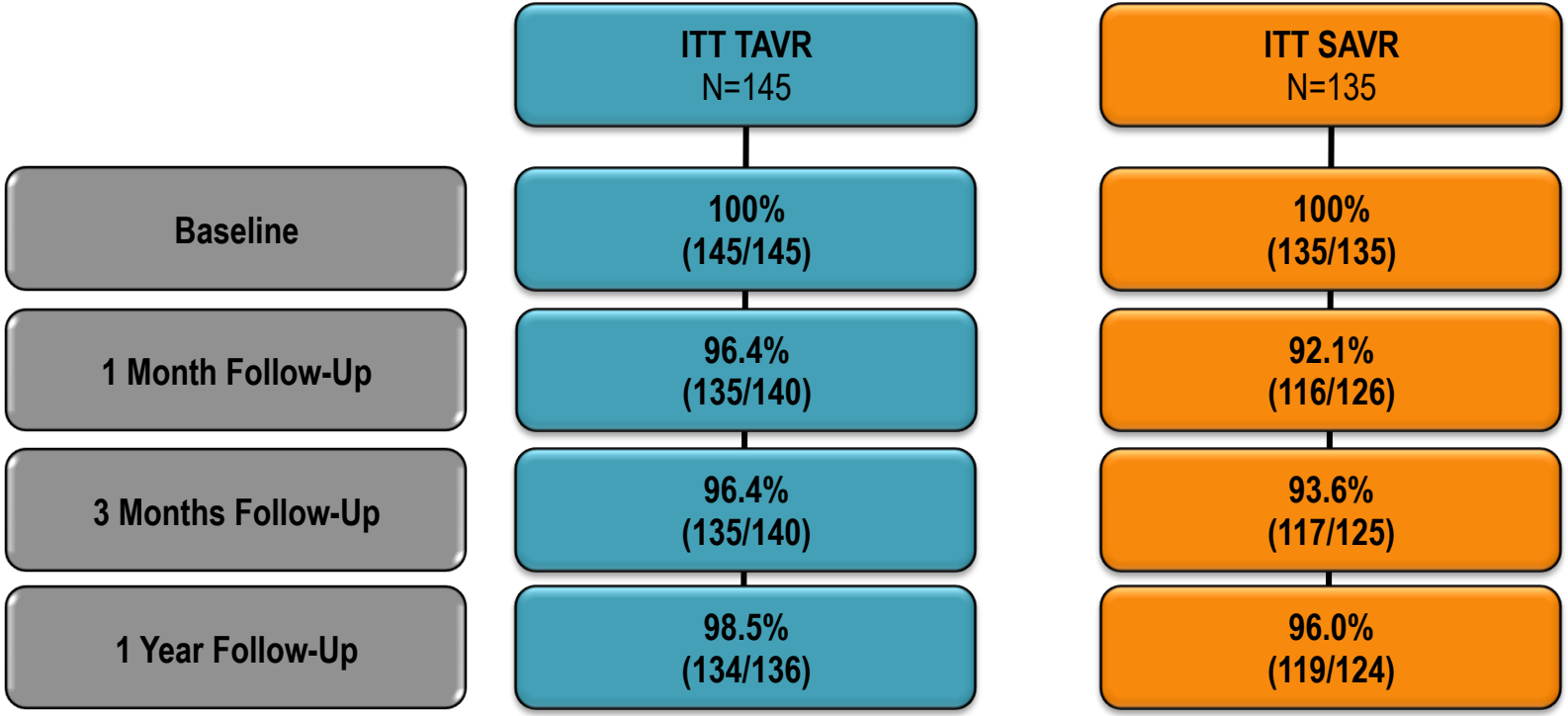
  All randomized patients.

  Patients were analyzed according to randomization, regardless of whether a procedure was actually attempted or which prosthesis was actually implanted.

Trial Flow


All randomized
n=280
ITT TAVR
n=145
ITT SAVR
n=135
Died prior to procedure
n=3
Crossover
TAVR to
SAVR
n=1
Crossover
SAVR to
TAVR
n=1
Died prior to procedure
n=1
AT TAVR
n=142
AT SAVR
n=134
Not implanted n=2
Crossover
TAVR to
SAVR
n=3
IMPLANTED
TAVR
n=139
IMPLANTED
SAVR
n=135

Trial Compliance



Baseline Characteristics

Characteristic, % or mean ± SD	TAVR n=145	SAVR n=135	p-value
Age (yrs)	79.2 ± 4.9	79.0 ± 4.7	0.71
Male	53.8	52.6	0.84
Society of Thoracic Surgeons (STS) Score	2.9 ± 1.6	3.1 ± 1.7	0.30
STS Score < 4%	83.4	80.0	0.46
Logistic EuroSCORE I	8.4 ± 4.0	8.9 ± 5.5	0.38
NYHA class III or IV	48.6	45.5	0.61

Baseline Characteristics, cont.

Characteristic, % or mean ± SD	TAVR n=145	SAVR n=135	p-value
Diabetes	17.9	20.7	0.55
Peripheral Vascular Disease	4.1	6.7	0.35
Prior Stroke	6.2	9.6	0.29
Chronic Obstructive Pulmonary Disease	11.7	11.9	0.97
Creatinine > 2 mg/dl	1.4	0.7	>0.99
Prior Myocardial Infarction	5.5	4.4	0.68
Prior Percutaneous Coronary Intervention	7.6	8.9	0.69

Primary Outcome*

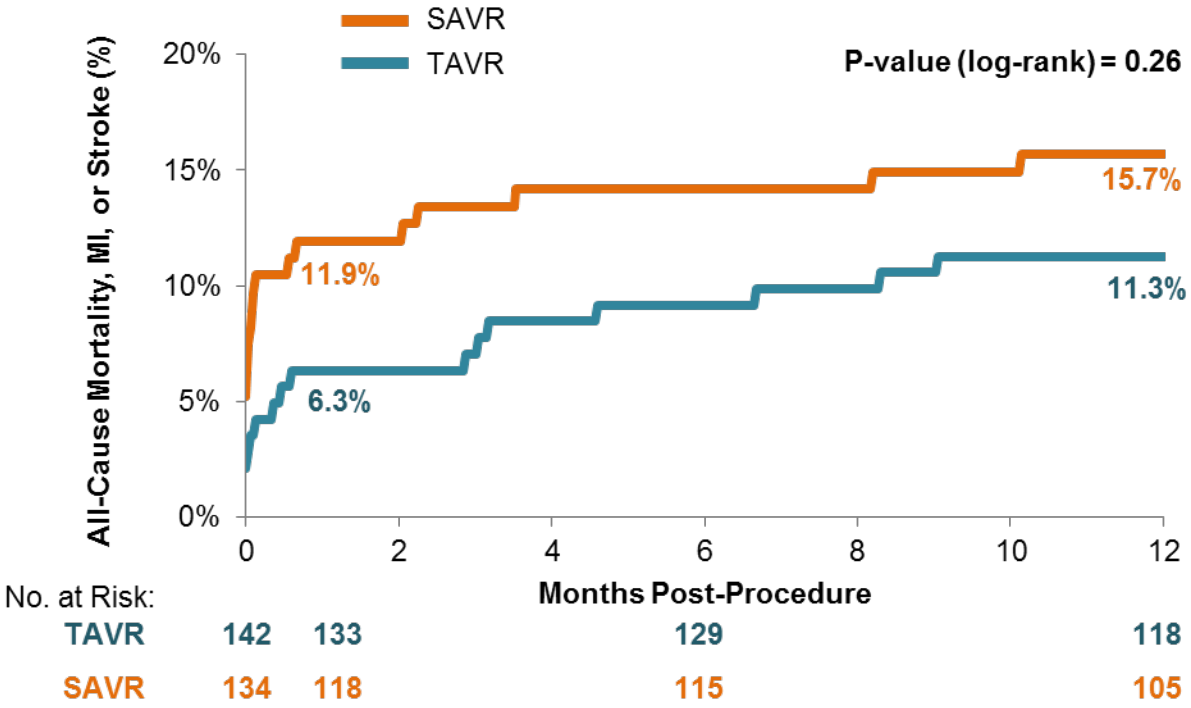
Composite rate of death from any cause, stroke or myocardial infarction 1 year after the procedure

TAVR 13.1% vs. SAVR 16.3%

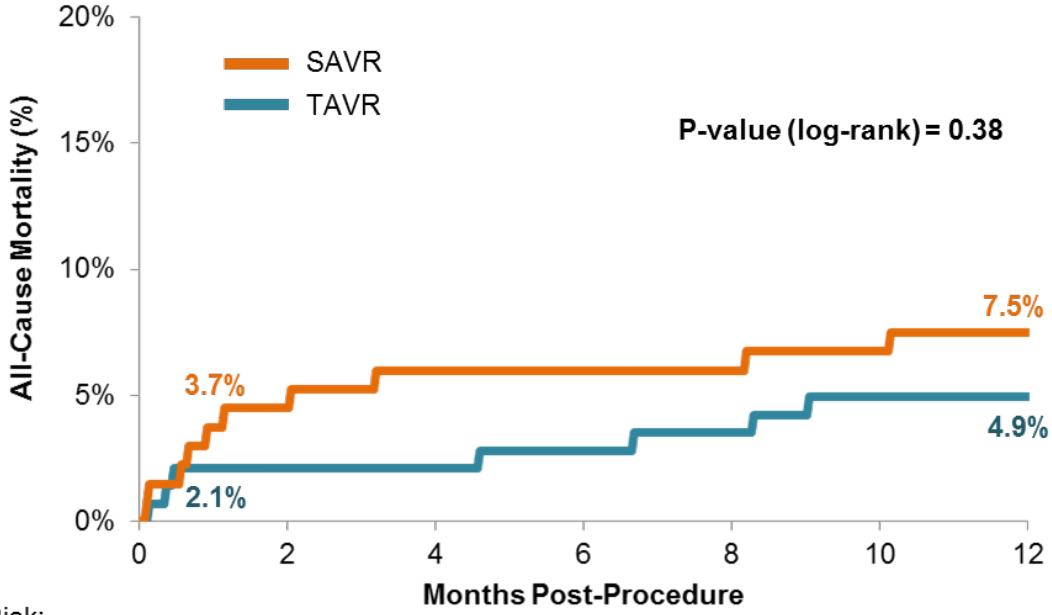
Absolute difference -3.2%; p=0.43 (for superiority)

*Intention-to-treat population

Death from Any Cause, Stroke or Myocardial Infarction at 1 Year in As-Treated Population



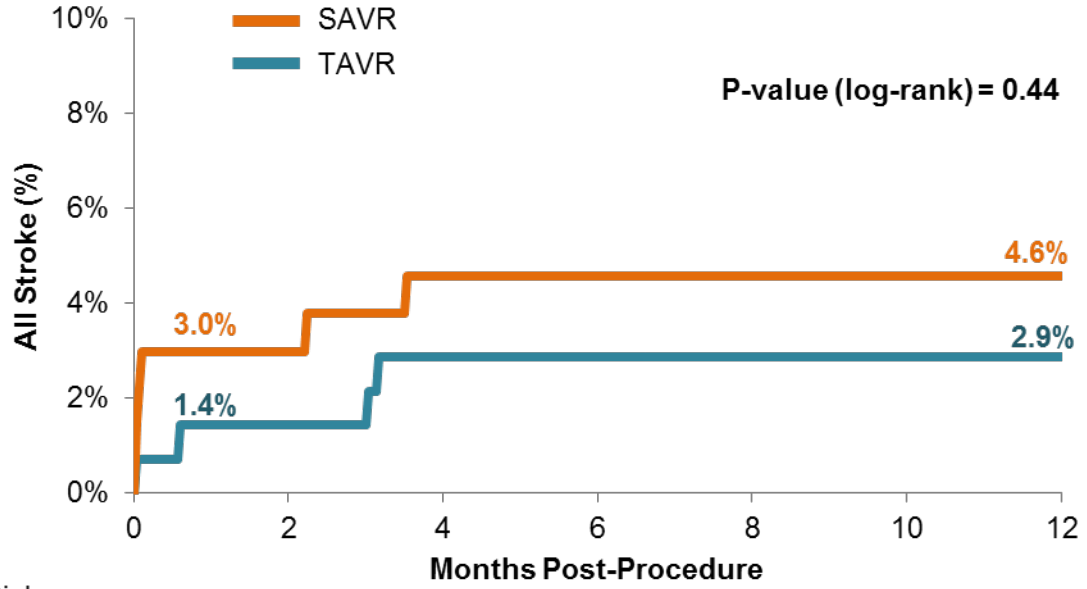
Death from Any Cause at 1 Year



No. at Risk:

TAVR	142	139	137	126
SAVR	134	128	125	115

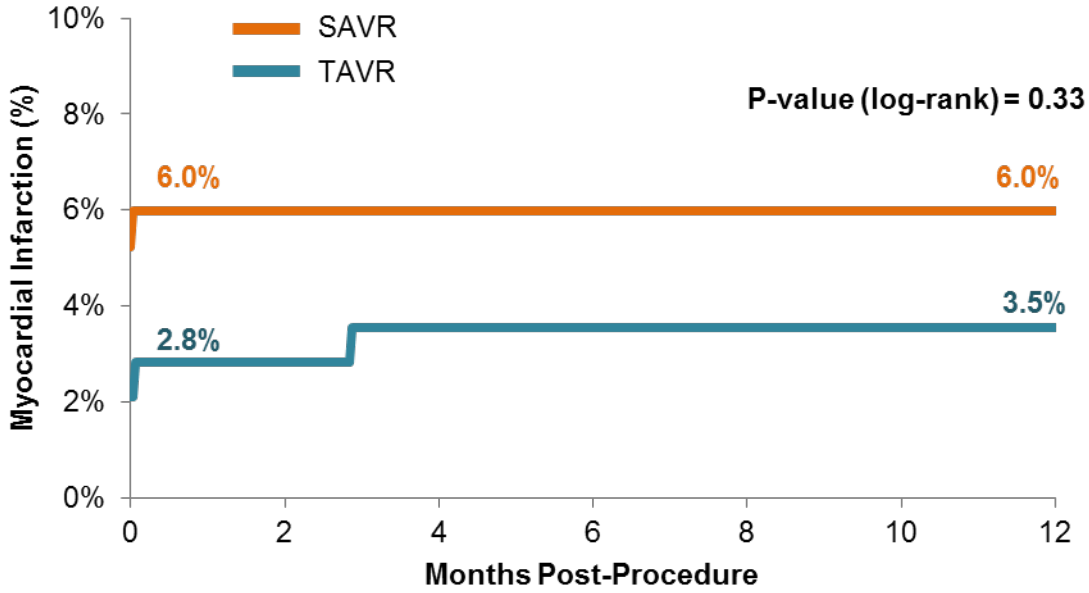
All Stroke at 1 Year



No. at Risk:

TAVR	142	137	134	123
SAVR	134	124	120	110

Myocardial Infarction at 1 Year



No. at Risk:

TAVR	142	135	132	121
SAVR	134	122	120	110

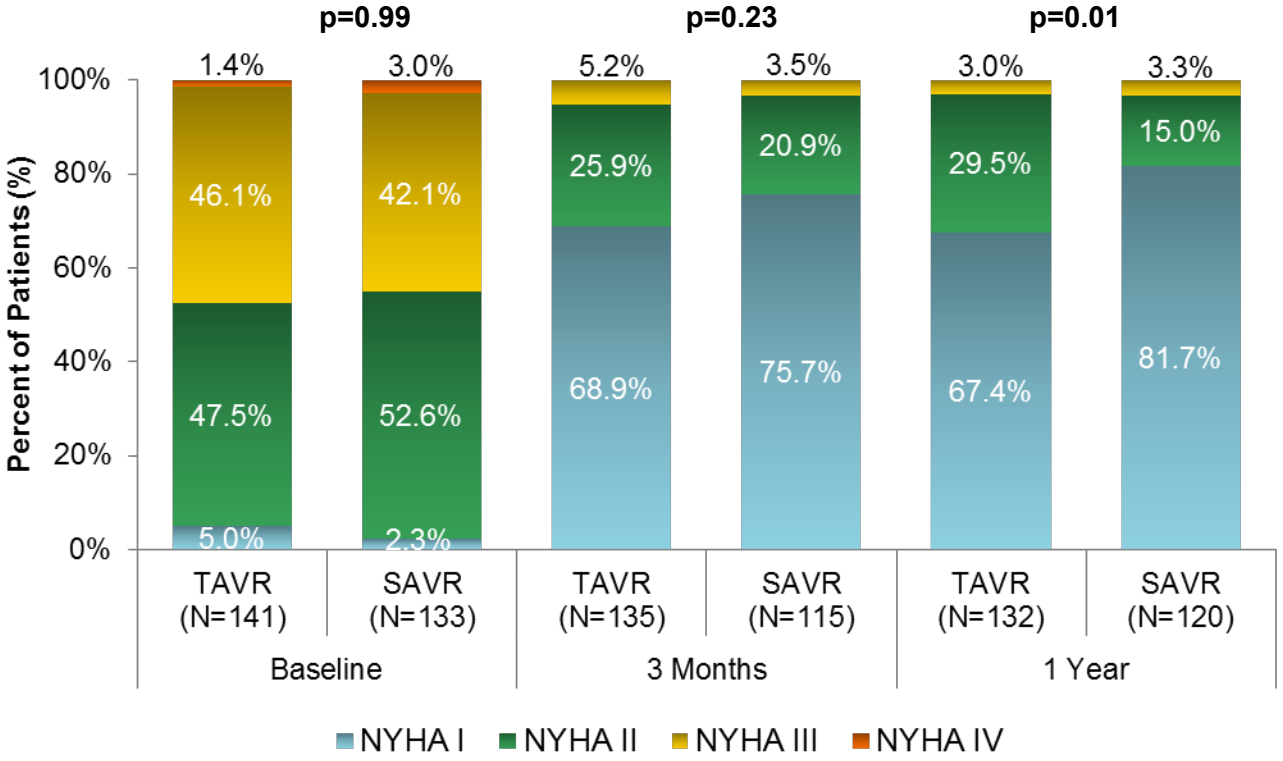
Secondary Outcomes at 30 Days

Outcome, %	TAVR n=142	SAVR n=134	p-value
Death, any cause	2.1	3.7	0.43
Death, cardiovascular	2.1	3.7	0.43
Bleeding, life-threatening+major	11.3	20.9	0.03
Cardiogenic shock	4.2	10.4	0.05
Vascular lesion, major	5.6	1.5	0.10
Acute kidney injury (stage II+III)	0.7	6.7	0.01
Stroke	1.4	3.0	0.37
TIA	1.4	0	0.17
Myocardial infarction	2.8	6.0	0.20
Atrial fibrillation	16.9	57.8	<0.001
Pacemaker	34.1	1.6	<0.001

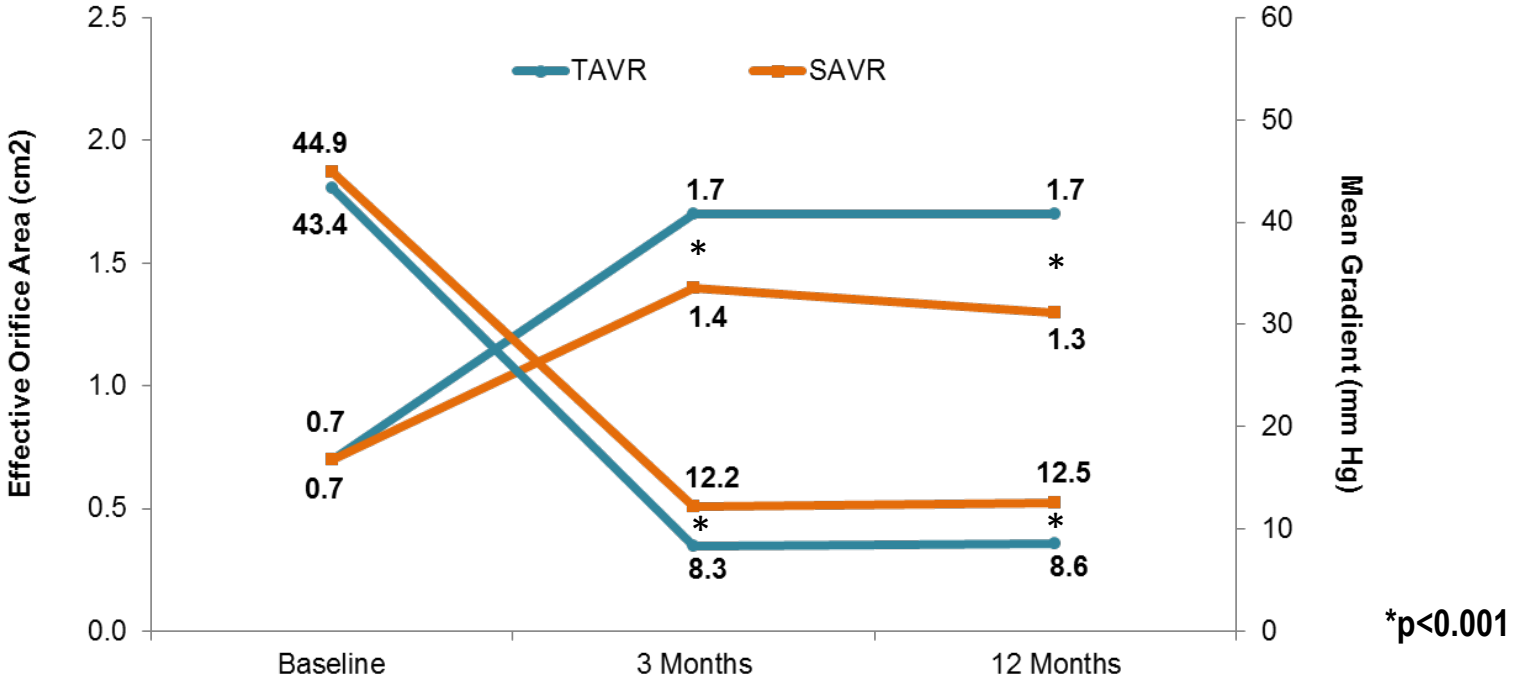
Secondary Outcomes at 1 Year

Outcome, %	TAVR n=142	SAVR n=134	p-value
Death, any cause	4.9	7.5	0.38
Death, cardiovascular	4.3	7.5	0.25
Stroke	2.9	4.6	0.44
TIA	2.1	1.6	0.71
Myocardial infarction	3.5	6.0	0.33
Atrial fibrillation	21.2	59.4	<0.001
Pacemaker	38.0	2.4	<0.001
Aortic valve re-intervention	0.0	0.0	na

NYHA Class in Survivors

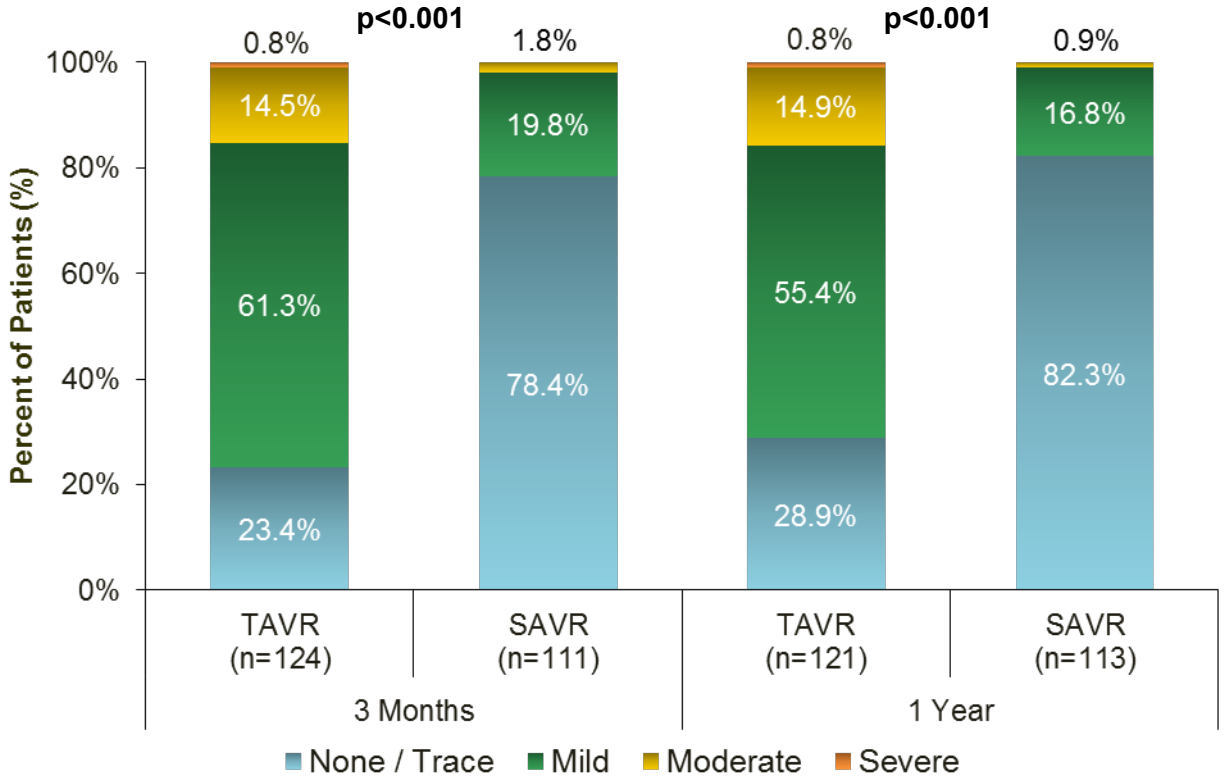


Aortic Valve Performance



*p<0.001

Aortic Valve Regurgitation



Conclusions

- The NOTION trial was the first all-comers trial to randomize low-risk patients to TAVR or SAVR
- TAVR was safe and effective, but not superior to SAVR regarding the composite rate of death from any cause, stroke or myocardial infarction after 1 year
- Procedural complications were different reflecting very different procedures
- Larger EOA and lesser gradients with TAVR prosthesis, but more regurgitation
- Long-term durability and morbidity data are required in lower risk patients