Treatment of High Risk Aortic Stenosis Patients with Transcatheter Medtronic CoreValve Implantation

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Disclosure Statements

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PI, Medtronic CoreValve ADVANCE Study

Medtronic CoreValve Proctor

customary travel and expenses only

CoreValve ADVANCE | Background

- Transcatheter Aortic Valve Implant (TAVI) enables treatment of aortic valve stenosis without open-heart surgery.

- Balloon-expandable TAVI
  - superior to standard medical therapy in inoperable patients
  - non-inferior to surgical AVR in high-risk patients with AS in a randomized controlled trial.

- Neither balloon-expandable or self expanding TAVI have been studied in a rigorous, monitored, independently adjudicated, 'real world' study.

Medtronic CoreValve® System

- Porcine pericardial tissue valve sutured into a self expanding nitinol frame
- Supra-annular valve function preserves circularity at level of valve function
- 18Fr catheter delivery system
- 3 valve sizes

CoreValve ADVANCE | Objective

The objective of the CoreValve ADVANCE study is to evaluate the

- safety
- efficacy
- clinical outcome according to VARC

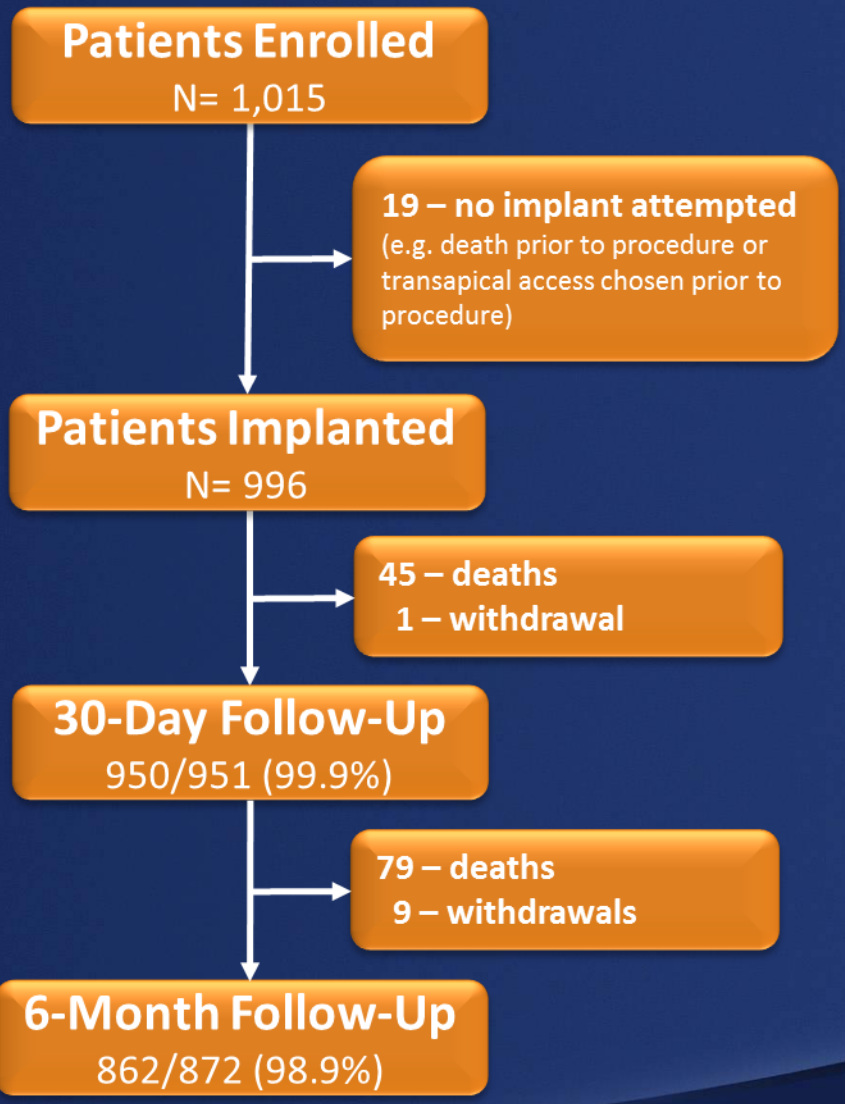
of percutaneous aortic valve implantation using the Medtronic CoreValve System in consecutive 'real world' patients with severe aortic stenosis considered

- inoperable or high risk

for conventional AVR by the local 'HEART TEAM'.

CoreValve ADVANCE | Methods

- 1,015 patients enrolled from March 2010 to July 2011
  - 5 year follow-up
- 44 centers - 12 countries in Western Europe, Asia and South America
- All centers had conducted at least 40 TAVI procedures prior to the study and had Heart Team in place
- Clinical endpoints reported according to Valve Academic Research Consortium (VARC)



CoreValve ADVANCE | Primary Endpoint

- **Primary Endpoint- Major Adverse Cardiac & Cerebrovascular Events (MACCE) at 30-days post procedure.**
  - MACCE defined as a composite of
    - All cause mortality
    - Myocardial Infarction (Q-wave and non-Q-wave)
    - Emergent cardiac surgery or percutaneous re-intervention
    - Stroke
- **Clinical endpoints reported according to VARC**
  - All-cause and Cardiovascular Mortality
  - Myocardial Infarctions
  - Stroke
  - Life Threating Bleeding
  - Major Vascular Complications
  - Acute Kidney Injury

CoreValve ADVANCE | Study Oversight

- 100% of all Patients were monitored
- All Primary Endpoint events adjudicated by an Independent Clinical Events Committee (CEC) Consisting of *TAVI-experienced* Interventional Cardiologists and Cardiac Surgeon
- All Cerebrovascular events adjudicated by an Independent Neurologist
  - Adjudication of events utilized all available relevant source documents; including neuroimaging and systematic NIH Stroke Scale assessments
- Core Laboratory
  - Systematic review and assessment of ECG's and Procedural Angiograms

CoreValve ADVANCE | Baseline Characteristics

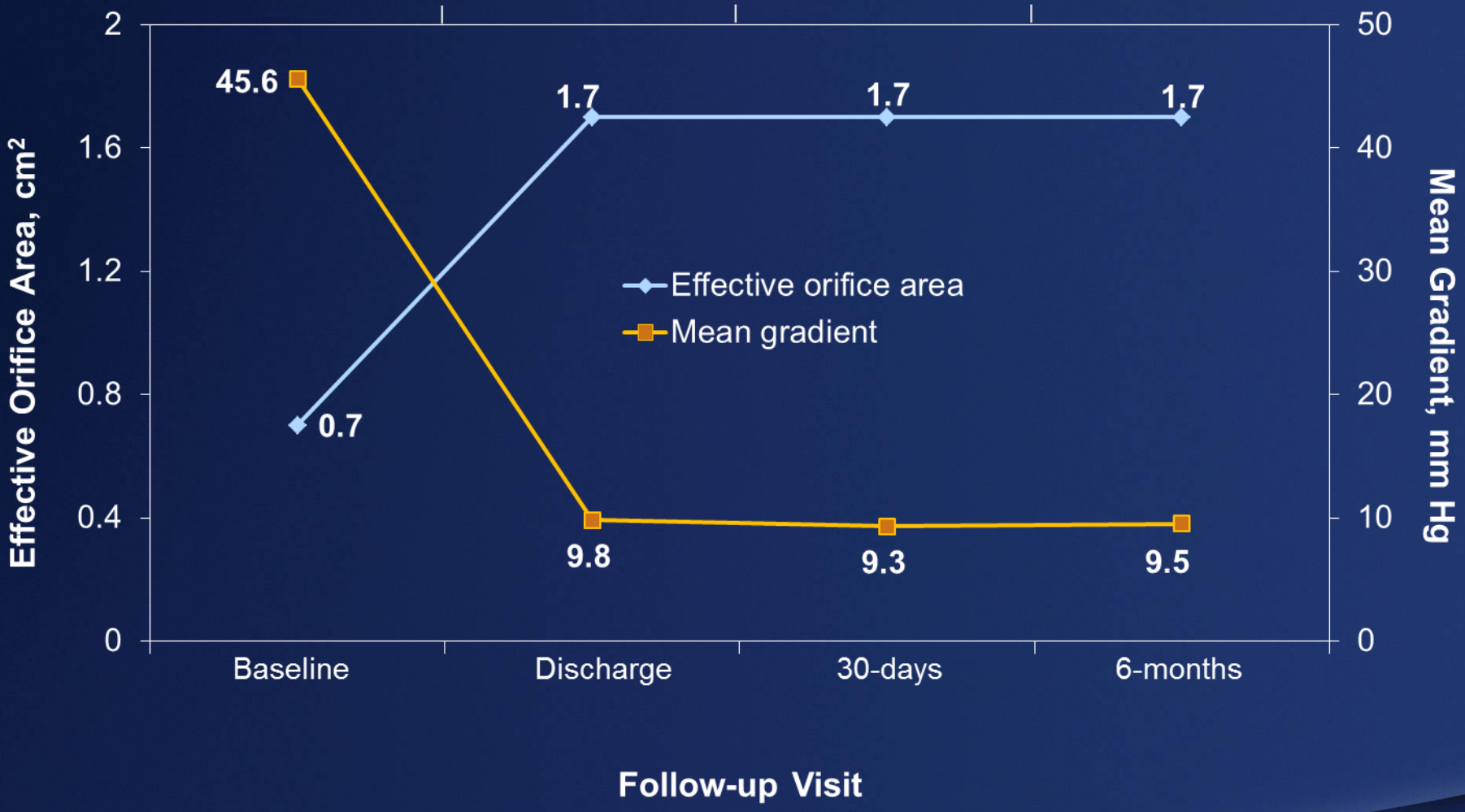
Characteristics	N=1015 %		%
Age (yrs.)	81 ± 6	Prior MI	16.0
Male	49.4	Prior PCI	31.1
Logistic EuroSCORE	19.2 ± 12.4	Permanent Pacemaker	12.8
NYHA		**EuroSCORE Relevant Factors**	
I or II	20.4	Prior CABG	21.4
III or IV	79.6	Cerebrovascular Disease	12.9
Diabetes	30.9	COPD	22.6
CAD	57.6	Pulmonary Hypertension	12.6
PVD	19.5	Prior median sternotomy	17.3
Atrial Fibrillation	32.8	Renal Failure	14.6

CoreValve ADVANCE | Procedural Results

Procedural Parameters N=996	%
Successful vascular access, delivery & deployment of device & successful retrieval of the delivery system	97.8
Correct position of the device in the proper anatomical location	98.7
Mean aortic valve gradient < 20 mmHg	96.2
No severe AR requiring intervention	97.9
Only one valve implanted in the proper anatomical location	96.0

Major Complications; Valve Related N=996	%
Annulus Rupture	0.0
Valve Embolization	0.3
Conversion to open AVR	0.1
Coronary Compromised	0.1

CoreValve ADVANCE | Valve Performance



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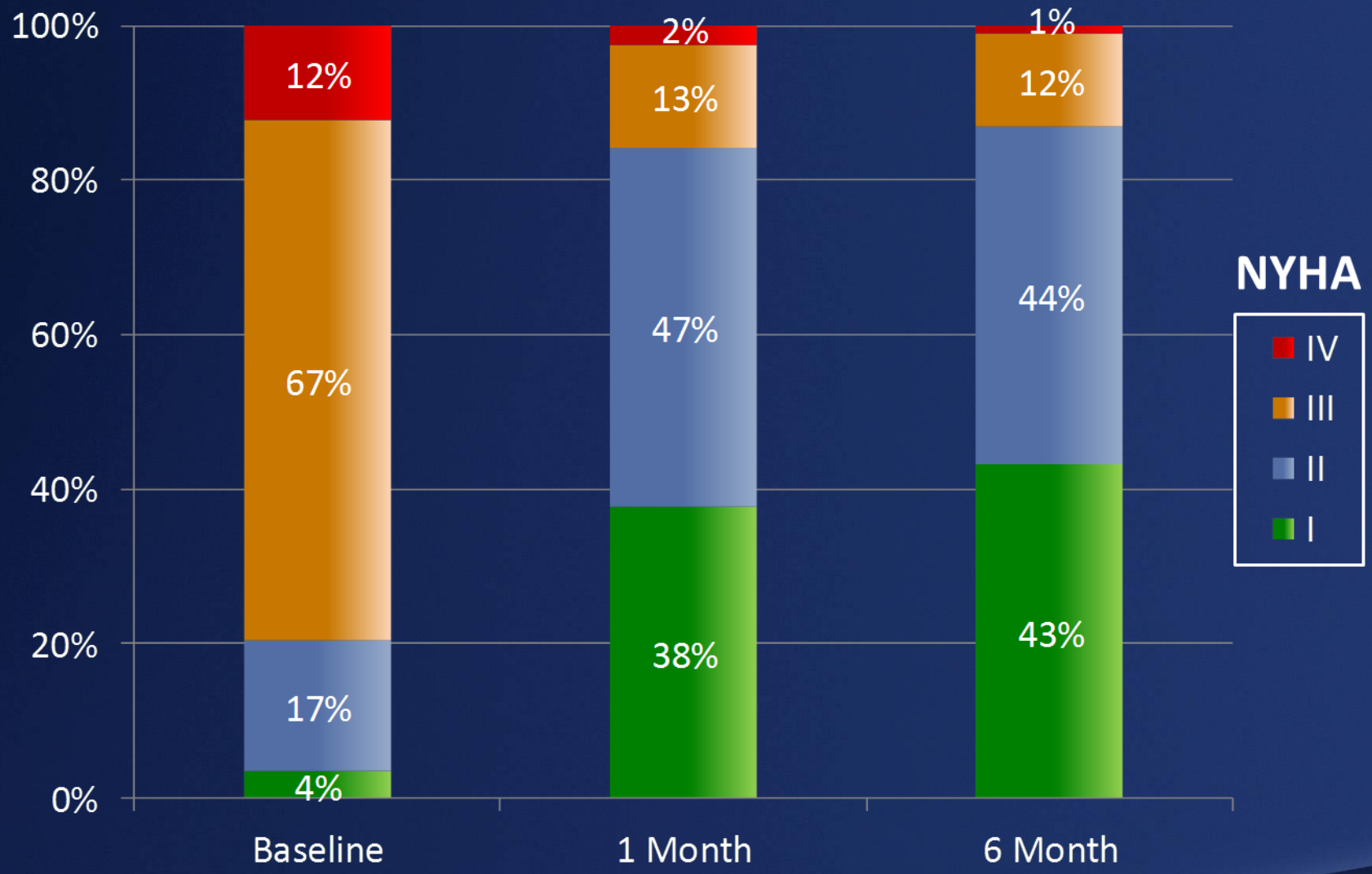
CoreValve ADVANCE | Symptom Status



CoreValve ADVANCE | 30-day Outcomes

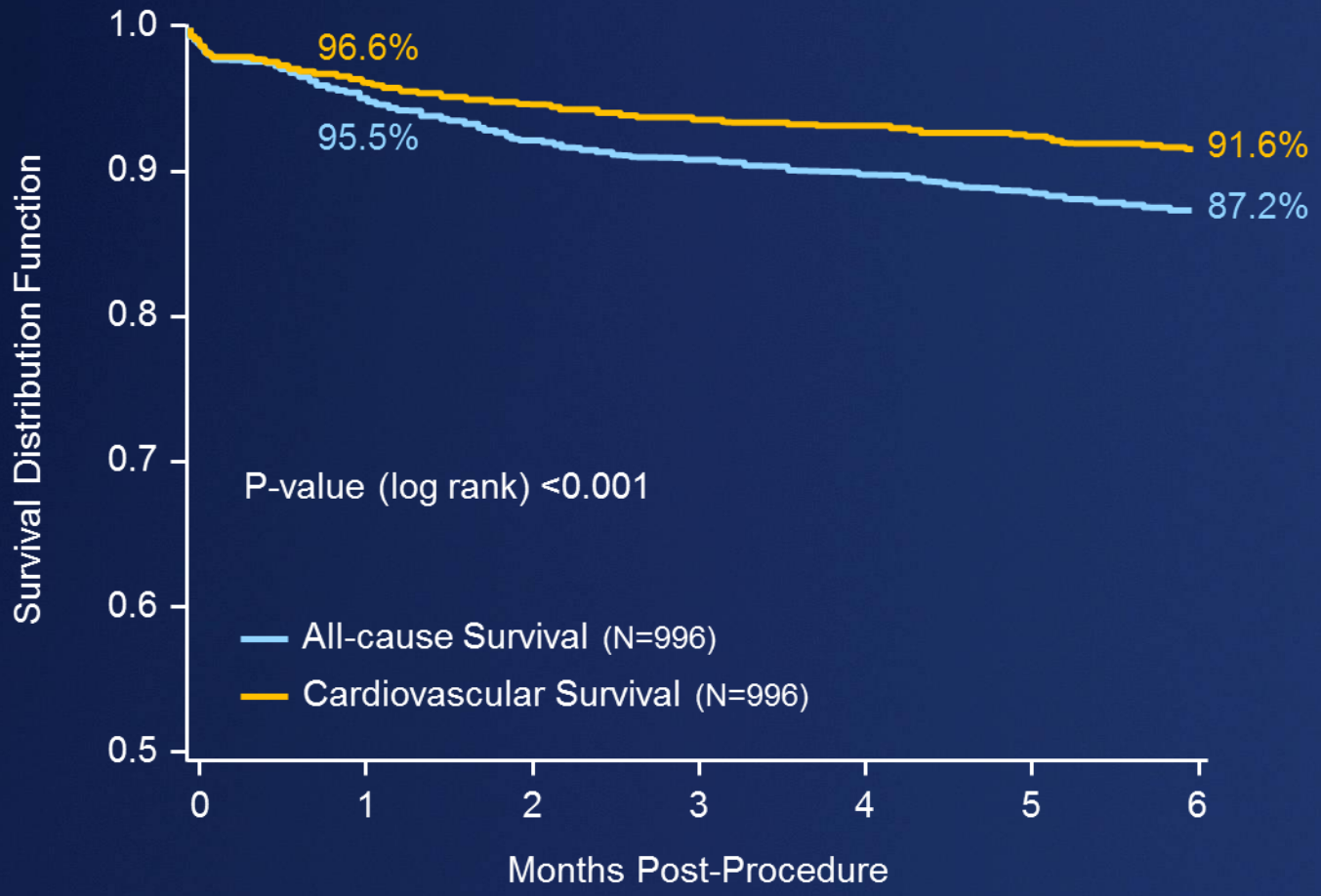
Primary Endpoint N=996	Kaplan-Meier Estimates, %
MACCE	8.3
All-cause Mortality	4.5
Myocardial Infarctions	0.2
Emergent cardiac surgery or percutaneous re-intervention	1.7
Stroke	2.9

Additional VARC Endpoints N=996	Kaplan-Meier Estimates, %
Cardiovascular Mortality	3.4
Major Bleeding	9.7
Life Threatening Bleeding	4.0
Major Vascular Complications	10.7
Acute Kidney Injury - Stage III	0.4

Additional Endpoint N=996	Kaplan-Meier Estimates, %
New Pacemaker Implantation	26.3

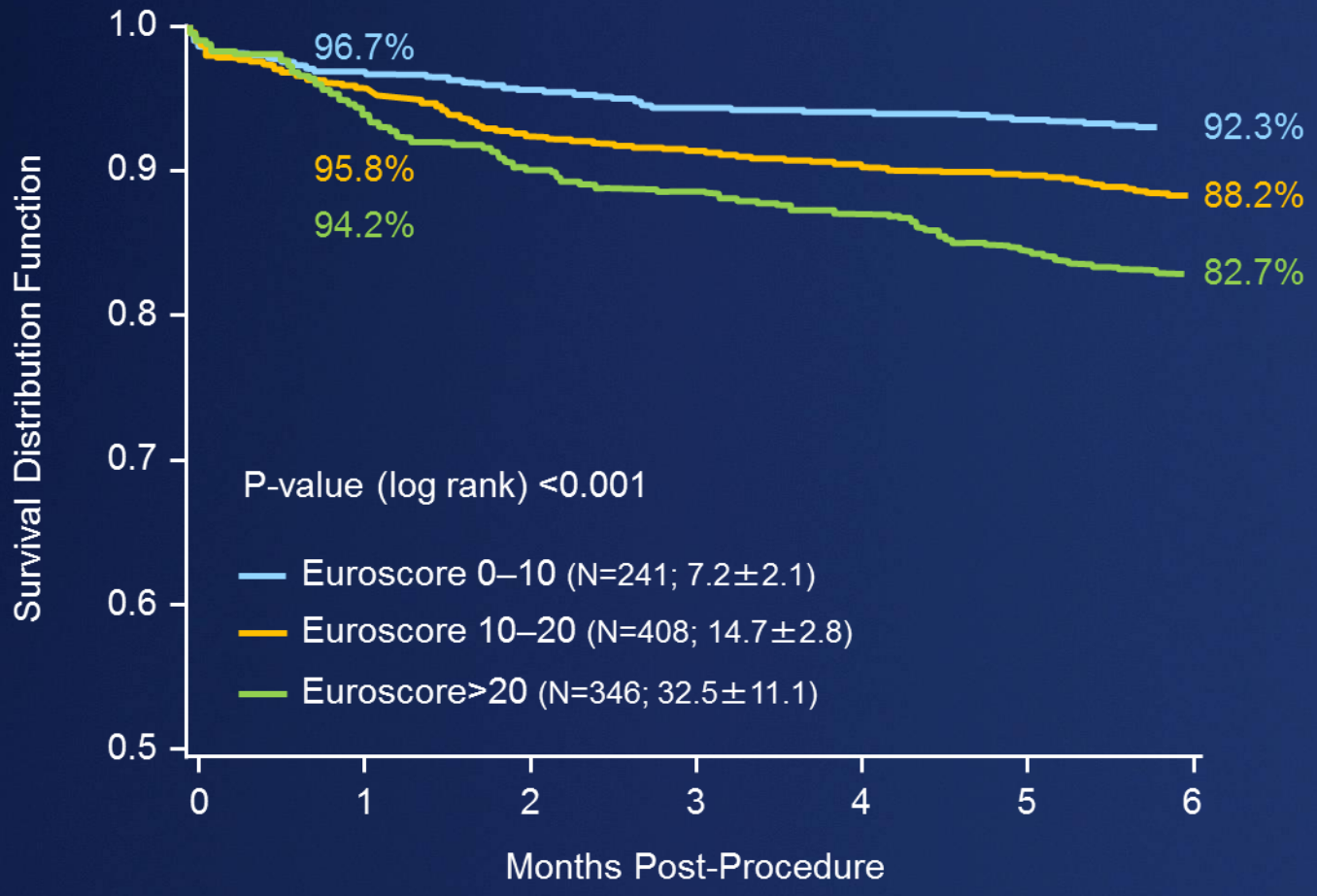
CoreValve ADVANCE | 6-month Survival

Kaplan-Meier Estimates of Freedom from **All-cause Mortality** (VARC) and **Cardiovascular Mortality** (VARC)



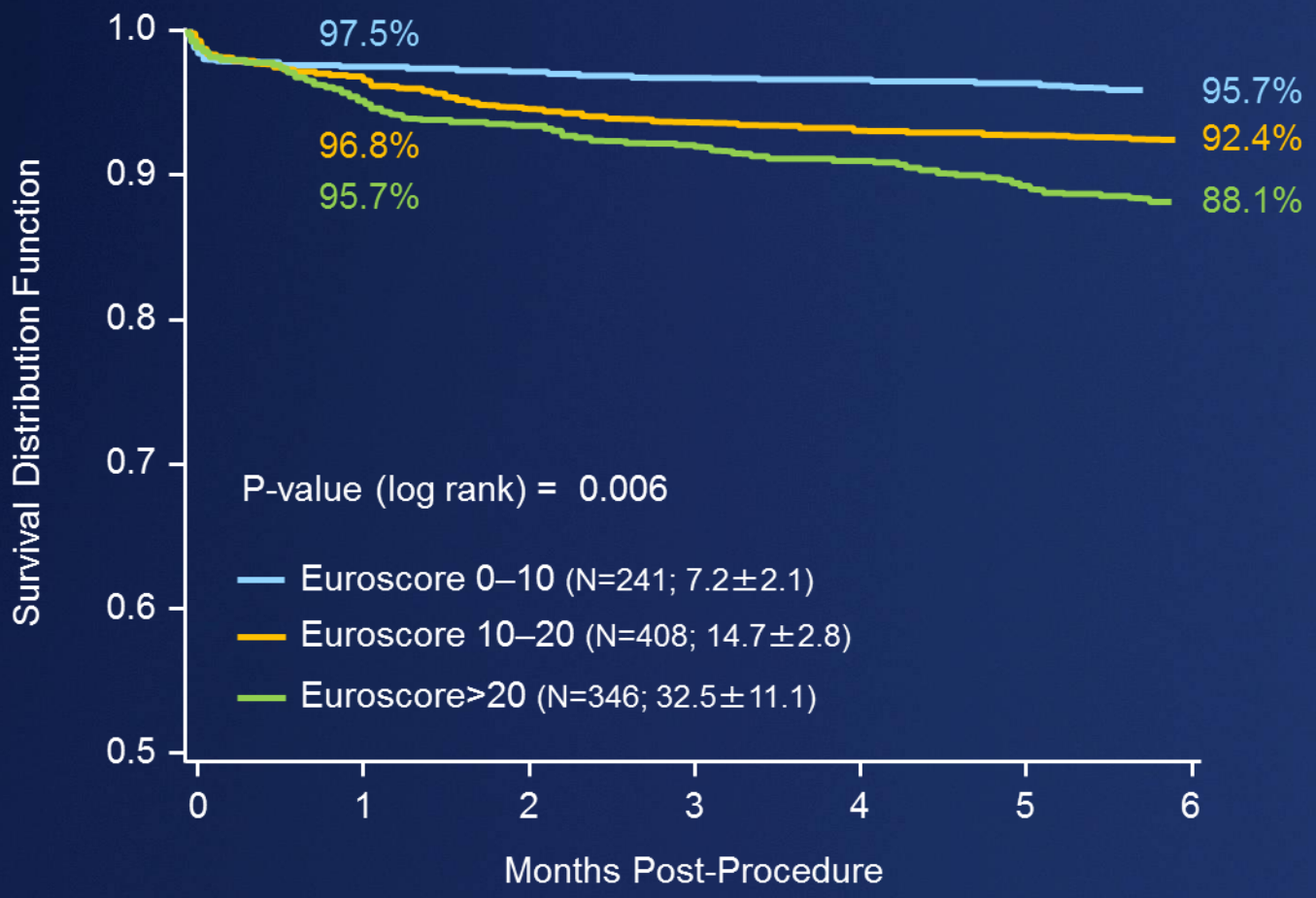
CoreValve ADVANCE | 6-month Survival

Kaplan-Meier Estimates of Freedom from **All-cause Mortality** by EuroSCORE group

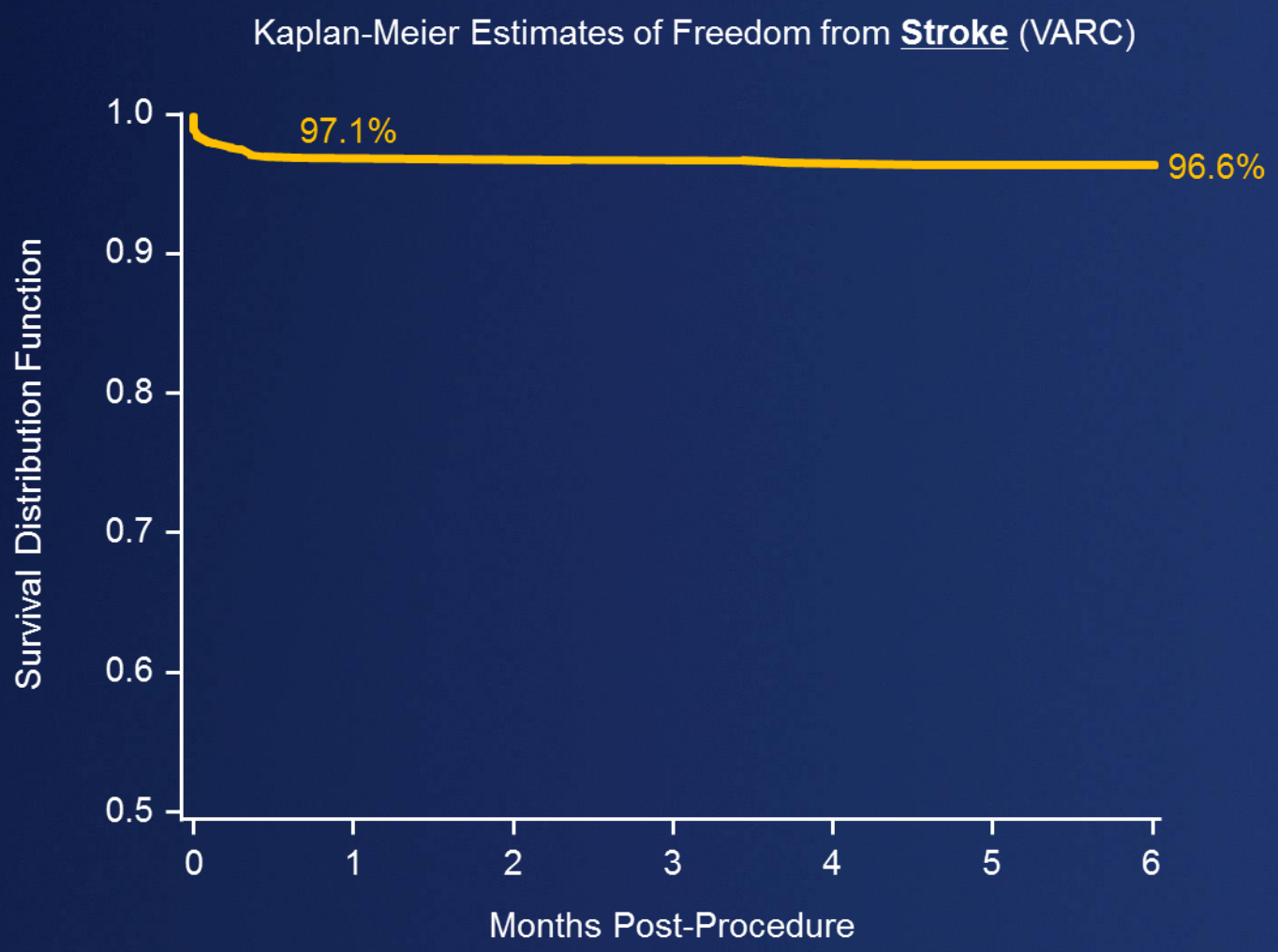


CoreValve ADVANCE | 6-month Survival

Kaplan-Meier Estimates of Freedom from **Cardiovascular Mortality** by EuroSCORE group



CoreValve ADVANCE | 6-month Stroke



Summary and Conclusions

- The CoreValve ADVANCE study, which is the largest, multicenter, prospective, fully monitored TAVI study, shows that treatment of 'real world' inoperable and frail, high-risk patients with the Medtronic CoreValve is:
  - Safe
  - Associated with:
    - an improvement in aortic valve function
    - low stroke and mortality rates at 1 month and 6 months follow-up

Thank You
CoreValve ADVANCE Study Centers

Hospital	# pts. enrolled
Universitat Leipzig Herzzentrum (DE)	100
Deutsches Herzzentrum Munchen (DE)	79
Leeds General Infirmary (UK)	57
Asklepios Klinik St. Georg Hamburg (DE)	54
Helios Klinikum Siegburg - Herzzentrum (DE)	49
Inselspital, University Hospital Bern (CH)	47
Azienda Ospedaliero Universitaria Policlinico Vittorio Emanuele di Catania (IT)	43
Rigshospitalet (DK)	39
CardioVascular Center Frankfurt (DE)	39
University Hospital Antwerp (BE)	36
Ospedale Niguarda Ca'Granda (IT)	35
Universitatsklinikum Aachen (DE)	32
Clinique Pasteur (FR)	30
Fondazione Centro San Raffaele (IT)	29
CHU Sart Tillman (BE)	29
Istituto Clinico S. Ambrogio (IT)	24
Groupe hospitalier Pitié-Salpêtrière (FR)	24
Immanuel Klinikum Bernau Herzzentrum Brandenburg (DE)	23
Hadassah Medical Center (IS)	20
Istituto Clinico Humanitas (IT)	20
Brighton and Sussex Hospital (UK)	18
Hôpital Cardiologique - CHRU de Lille (FR)	18

Hospital	# pts. enrolled
Amphia Hospital Breda (NL)	18
St. George`s Hospital (UK)	15
Tel Aviv Sourasky Medical Center (IS)	14
St. Antonius Hospital Nieuwegein (NL)	12
ZNA Antwerpen Middelheim (BE)	10
Newcross Hospital Wolverhampton (UK)	9
University Hospital Zürich (CH)	8
Ospedale Civile (IT)	8
Catharina Hospital Eindhoven (NL)	8
Hospital de Santa Cruz Centro Hospitalar de Lisboa Ocidental (PT)	7
The Heart Hospital (UK)	7
Glenfield Hospital (UK)	6
Angiografia de Occidente (CO)	6
Hopital Henri Mondor (FR)	6
Hopital Louis Pradel (FR)	6
Centro Hospitalar de Vila Nova de Gaia (PT)	5
The Chaim Sheba Medical Center (IS)	5
Azienda Ospedaliere Spedali Civili di Brescia (IT)	5
AMC Hospital (NL)	5
Azienda Ospedaliero Universitaria Careggi (IT)	4
Institut Hospitalier Jacques Cartier (FR)	4
Onassis Cardiac Surgery Center (GR)	2

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