Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010. DOI: 10.1056/NEJMoa1008232.

TABLES AND FIGURES (SUPPLEMENTARY APPENDIX)

Table 1: PARTNER Inclusion and Exclusion Criteria

Inclusion Criteria

1. Senile degenerative aortic valve stenosis with echocardiography derived criteria: mean gradient > 40 mm Hg or jet velocity > 4.0 m/s or an aortic valve area (AVA) of < 0.8 cm^2 (or AVA index < 0.5 cm^2/m^2).
2. Symptomatic due to aortic valve stenosis as demonstrated by NYHA Functional Class ≥ II.
3. The subject or the subject's legal representative was informed of the nature of the study, agreed to its provisions and provided written informed consent as approved by the Institutional Review Board of the respective clinical site.
4. The subject and the treating physician agreed that the subject would return for all required post-procedure follow-up visits.
5. The subject, after formal consults by a cardiologist and two cardiovascular surgeons agreed that medical factors precluding operation, based on a conclusion that the probability of death or serious, irreversible morbidity exceeded the probability of meaningful improvement. Specifically, the probability of death or serious, irreversible morbidity exceeded 50%. The surgeons' consult notes should specify medical or anatomic factors leading to that conclusion and included should be a printout of the STS score calculation to further identify the risks in these patients.

Exclusion Criteria

1. Evidence of an acute myocardial infarction ≤ 1 month before the intended treatment (defined as Q wave MI, or non-Q wave MI with total CK elevation ≥ twice normal in the presence of CK-MB elevation and/or troponin level elevation (WHO definition).
2. Aortic valve was a congenital unicuspid or congenital bicuspid valve, or was non-calcified.
3. Mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation >3+).

4. Any therapeutic invasive cardiac procedure performed within 30 days of the index procedure, (or 6 months if the procedure was a drug eluting coronary stent implantation).
5. Pre-existing prosthetic heart valve in any position, prosthetic ring, severe mitral annular calcification, or severe (greater than 3+) mitral regurgitation
6. Blood dyscrasias as defined: leukopenia (WBC < 3000 mm^3), acute anemia (Hb < 9 mg%), thrombocytopenia (platelet count < 50,000 cells/mm^3), history of bleeding diathesis or coagulopathy.
7. Untreated clinically significant coronary artery disease requiring revascularization.
8. Hemodynamic instability requiring inotropic therapy or mechanical hemodynamic support devices.
9. Need for emergency surgery for any reason.
10. Hypertrophic cardiomyopathy with or without obstruction.
11. Severe ventricular dysfunction with LVEF < 20%.
12. Echocardiographic evidence of intracardiac mass, thrombus or vegetation.
13. Active peptic ulcer or upper gastro-intestinal bleeding within the prior 3 months.
14. A known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media, which cannot be adequately pre-medicated.
15. Native aortic annulus size < 18mm or > 25mm as measured by echocardiogram.
16. Recent (within 6 months) cerebrovascular accident or transient ischemic attack.
17. Renal insufficiency (creatinine > 3.0mg/dL) and/or end stage renal disease requiring chronic dialysis.
18. Life expectancy < 12 months due to non-cardiac co-morbid conditions.
19. Significant abdominal or thoracic aorta disease, including aneurysm (defined as maximal luminal diameter 5cm or greater), marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding or ulcerated), narrowing of the abdominal aorta (especially with calcification and surface irregularities), or severe “unfolding” and tortuosity of the thoracic aorta
20. Iliofemoral vessel characteristics that would preclude safe placement of 22F or 24F introducer sheath such as severe calcification, severe tortuosity or vessels size diameter < 7 mm for 22F sheath or < 8mm for 24F sheath.

21. Currently participating in an investigational drug or another device study.

22. Active bacterial endocarditis or other active infections.

23. Bulky calcified aortic valve leaflets in close proximity to coronary ostia.

AVA denotes aortic valve area, Hb hemoglobin, LVEF left ventricular ejection fraction, MI myocardial infarction, NYHA New York Heart Association, STS Society of Thoracic Surgeons, WBC white blood cells.

Table 2: PARTNER Study Organization

Executive Committee	M.B. Leon, (Co-Principal Investigator), Columbia University Medical Center, New York; C. Smith, (Co-Principal Investigator), Columbia University Medical Center, New York; M. Mack, Medical City Dallas, Dallas; D.C. Miller, Stanford University Medical Center, Palo Alto; J. Moses, (Co-Chairman, Publication Committee), Columbia University Medical Center, New York; L. Svensson, (Co-Chairman, Publication Committee), Cleveland Clinic Foundation, Cleveland; M. Tuzcu, Cleveland Clinic Foundation, Cleveland; J. Webb, St. Paul's Hospital, Vancouver, BC.
Site monitoring	Edwards Lifesciences, LLC, Irvine, CA: N. Cohen (Director); Bright Pharmaceutical Services, Inc., Sherman Oaks, CA.
Electronic Database	RAVE, Medidata Systems, New York, NY.
Data management	Edwards Lifesciences, LLC, Irvine, CA: G. Dziem (Director); W.N. Anderson (Consultant), Lake Forest, CA.
Biostatistics	London School of Hygiene and Tropical Medicine: S. Pocock, D. Wang; W.N. Anderson (Consultant), Lake Forest, CA.
DSMB	J. Carrozza (Chairman), Harvard Medical School, Boston, MA; Committee Members: A. Wechsler, Philadelphia, PA; B. Carabello, Houston, TX; E. Peterson, Durham, NC; K. Lee, Durham, NC.
Safety Officer	Edwards Lifesciences, LLC, Irvine, CA: S. Bartus (Manager)
CEC	J. Petersen (Chairman), Duke Clinical Research Institute, Durham, NC
Echocardiography and ECG Core Lab.	P. Douglas (Principal Investigator), Duke Clinical Research Institute, Durham, NC.
Economic and Quality of Life Core Lab.	D. Cohen (Principal Investigator), Mid-America Medical Center, Kansas; M. Reynolds (Director), Harvard Clinical Research Institute, Boston, MA. and St. Luke's Medical Center, Kansas City, MO.

CEC denotes clinical events committee, DSMB data safety monitoring board, ECG electrocardiogram, Lab laboratory.

Table 3. PARTNER Endpoint Definitions According to the Clinical Events Committee Charter (major endpoints)

1. Death

All events, including deaths were reviewed once as a blinded review and then as an unblinded review. During the unblinded review, deaths were evaluated to determine if the event was related to the valve and/or procedure. Deaths were sub-classified into cardiovascular, non-cardiovascular, or unknown.

Cardiovascular: Deaths resulting from a cardiac cause. This category included valve-related deaths, (including sudden unexplained deaths) and non-valve related cardiac deaths (e.g., congestive heart failure [CHF], acute myocardial infarction [MI], documented fatal arrhythmias) in which a cardiac cause could not be excluded. All cardiovascular deaths were sub-classified into the following categories: sudden, unexpected and unexplained death, CHF, MI, arrhythmia, endocarditis of prosthetic study valve, central nervous system (CNS) event, non-cerebral hemorrhage, peripheral arterial embolism, vascular complication, peripheral arterial disease, valve-related, procedure-related, and other. Deaths directly related to the procedure or complications thereof or any death occurring ≤ 30 days after the procedure were classified as procedure related.

Non-Cardiovascular: Defined as a death not due to cardiac causes (as defined above). All non-cardiac deaths were sub-classified into the following categories: malignancy, accidental, infection/sepsis, renal disease, or other (e.g., hepatic failure, diabetes, congestive obstructive pulmonary disease [COPD]).

2. Myocardial Infarction

All myocardial infarctions (MIs) were adjudicated for device and procedural relationship. Any of the following criteria met the definition of MI:

(1) any acute MI demonstrated by autopsy,

(2) any emergent PCI performed for acute ST-elevation myocardial infarction,

(3) any administration of thrombolytics for acute myocardial infarction,

(4) periprocedural MI occurred through 7 days post index procedure and was defined as follows:

- Periprocedural Q-wave MI: development of new pathologic Q waves in 2 or more contiguous leads with elevation of CK-MB or CK in absence of CK-MB data. New Q waves in the absence of symptoms or elevated markers were not considered an MI.
- Periprocedural Non-Q-wave MI: Documented signs or symptoms of ischemia and/or new ischemic changes on ECG **and** CK-MB elevation > 10 X ULN. In the absence of CK-MB data, CK was used.

(5) non-procedural MI occurred after 7 days post index procedure and was defined as follows:

- Q-wave MI: development of new pathologic Q waves in 2 or more contiguous leads with elevation of CK, CK-MB or troponin in clinical setting with signs or symptoms of myocardial ischemia.
- Non-Q-wave MI: elevation of CK > 2 times ULN with elevation of CK-MB or troponin in clinical setting with signs or symptoms of myocardial ischemia.

3. CNS (neurologic) Events

TIA was defined as a focal neurologic event that was fully reversible in < 24 hours in the absence of any new imaging findings of infarction or other primary medical cause (hypoglycemia, hypoxia, etc).

A stroke was defined as follows:

- Focal neurologic deficit lasting ≥ 24 hours OR
- Focal neurologic deficit lasting < 24 hours with imaging findings of acute infarction or hemorrhage.

Stroke was further classified as ischemic, hemorrhagic (epidural, subdural, subarachnoid), or ischemic with hemorrhagic conversion.

A minor stroke was defined as an event associated with a modified Rankin Scale of 0 or 1 at 30 days or longer after the event. This was determined by review of the source documentation surrounding the stroke, including but not limited to progress notes, consult notes, discharge summaries and follow-up

clinic notes. If NIH Stroke Scale was available, this was considered by the committee. A NIH stroke scale score of 0 was considered a minor stroke.

A major stroke was defined as a stroke associated with a modified Rankin Scale of 2 or greater at 30 days or longer after the event. If NIH Stroke Scale information was available, this was incorporated into the adjudication.

4. Vascular Complications

Vascular complications were classified as access site hematoma (size >5 cm), access site false (pseudo) aneurysm, arterio-venous fistula, retroperitonal bleeding, peripheral nerve injury, vascular perforation, vascular dissection, or mesenteric ischemia. Vascular events were categorized according to a modified version of the VARC classification[35] into either minor or major vascular complications. Any event which was not a major complication was considered a minor event.

Major vascular complications were defined as follows: (1) any thoracic aortic dissection, (2) access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, or compartment syndrome) leading to either death, need for significant blood transfusions (> 3 units), unplanned percutaneous or surgical intervention, or irreversible end-organ damage (e.g., hypogastric artery occlusion causing visceral ischemia or spinal artery injury causing neurologic impairment), (3) distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage, or (4) left ventricular perforation.

5. Bleeding Events

Bleeding events were classified as either major or minor.

Major Bleeding defined as a clear site of bleeding that met any one of the following criteria: (1) bleeding that caused death, (2) bleeding that caused a hospitalization or prolonged hospitalization ≥ 24 hours due to treatment of bleeding, (3) required pericardiocentesis or open and/or endovascular procedure for repair

or hemostasis, (4) caused permanent disability (e.g. blindness, paralysis, hearing loss), (5) required transfusion of > 3 units of blood within 24 hour period.

Minor Bleeding had to meet all of the following criteria: (1) bleeding event that did not meet criteria for major bleeding, (2) clear site for bleeding, (3) loss of hemoglobin > 3 g/dL or loss of hematocrit > 9%. Adjustment for transfusions was included at 1 g/dL or 3% for each unit of blood.

6. Acute Renal Injury

Renal failure events were defined as chronic dialysis of any sort (hemodialysis, CVVHD, peritoneal) for a duration of greater than 30 days. The date of event was based on the date of the first treatment with renal replacement therapy. Patients who died before 30 days were not considered renal failure events. In addition, any episode of renal replacement therapy, either transient or greater than 30 days duration, was reviewed and assessed for device and procedural relationship.

7. Repeat Hospitalization for Valve or Procedure-Related Clinical Deterioration

The clinical event committee (CEC) assessed all repeat hospitalizations for symptoms of aortic stenosis (valve-related deterioration) or for complications associated with the valve procedure.

- ***Repeat hospitalization due to aortic stenosis*** was defined as symptoms of aortic stenosis including heart failure, angina or syncope due to aortic valve disease requiring aortic valve intervention or intensified medical management. Repeat hospitalization for CHF was defined as hospitalization AND clinical symptoms of CHF with objective signs including pulmonary edema, hypoperfusion or documented volume overload AND administration of IV diuresis or inotropic therapy, performance of aortic valvuloplasty, institution of mechanical support (IABP or ventilation for pulmonary edema) or hemodialysis for volume overload. Administration of IV therapies in the clinic or in the Emergency Department without admission did not qualify as hospitalization events. Repeat hospitalization for angina not related to CAD was defined as hospitalization AND clear documentation of anginal symptoms AND no clinical evidence that angina was related to CAD or

ACS. Repeat hospitalization for syncope was defined as hospitalization AND documented loss of consciousness not related to seizure or tachyarrhythmia.

- ***Repeat hospitalization for complications of the valve procedure*** was defined as any hospitalization which could be associated with the aortic valve procedure including infectious complications, stroke, renal failure, and vascular complications. Repeat hospitalization for infectious complications included any infectious complication resulting directly from the access site or involving the aortic valve (mechanical or native). Repeat hospitalization for renal failure included progressive renal insufficiency resulting in the need for renal replacement therapy. Repeat hospitalization for stroke was defined as any stroke which may have been related to an aortic valve procedure. Repeat hospitalization for vascular complications was defined as hospitalization for any arterial vascular access complication related to performing an aortic valve procedure.

Table 4. Causes of Death

	TAVI (N=179)		Control (N=179)	
	no. (%)		no. (%)	
Cause Death	**≤ 30 days**	**> 30 days**	**≤ 30 days**	**> 30 days**
All	**9 (5.0%)**	**62 (34.6%)**	**5 (2.8%)**	**102 (57.0%)**
Cardiovascular	**7 (3.9%)**	**20 (11.2%)**	**3 (1.7%)**	**56 (31.3%)**
Congestive heart failure	2 (1.1%)	8 (4.5%)	1 (0.6%)	30 (16.8%)
Sudden, unexpected or unexplained	1 (0.6%)	3 (1.7%)	1 (0.6%)	17 (9.5%)
Central nervous system event	2 (1.1%)	2 (1.1%)	0 (0.0%)	4 (2.2%)
Arrhythmia	0 (0.0%)	0 (0.0%)	1 (0.6%)	2 (1.1%)
Vascular complication	2 (1.1%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
Endocarditis of study vale	0 (0.0%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
Non-cerebral hemorrhage	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.1%)
Myocardial infarction	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.6%)
Peripheral arterial disease/abdominal aortic aneurysm	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
Unknown cardiovascular	0 (0.0%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
Non Cardiovascular	**1 (0.6%)**	**26 (14.5%)**	**2 (1.1%)**	**13 (7.3%)**
Infection/sepsis	1 (0.6%)	8 (4.5%)	2 (1.1%)	5 (2.8%)
Malignancy	0 (0.0%)	4 (2.2%)	0 (0.0%)	4 (2.2%)
Renal disease	0 (0.0%)	3 (1.7%)	0 (0.0%)	1 (0.6%)
Accidental	0 (0.0%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
Other	0 (0.0%)	8 (4.5%)	0 (0.0%)	3 (1.7%)
Unknown non-cardiovascular	0 (0.0%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
Unknown	**1 (0.6%)**	**16 (8.9%)**	**0 (0.0%)**	**33 (18.4%)**

TAVI denotes transcatheter aortic valve implantation.

Table 5. Analysis of Neurologic Events (up to 1 year follow-up)

Event	Time-to-Event (Days)+	Therapy	Etiology	Death
TIA	145	TAVI	Unknown	No
Stroke - Minor	3	Control	Ischemic	No
Stroke - Minor	5	TAVI	Ischemic	No
Stroke - Minor	1	TAVI	Ischemic	No
Stroke - Minor	2	TAVI	Ischemic	No
Stroke - Minor	75	TAVI	Ischemic	No
Stroke - Major	48	Control	Ischemic	Yes
Stroke - Major	62	Control	Ischemic	Yes
Stroke - Major	14	Control	Unknown	No
Stroke - Major	172	Control	Ischemic	No
Stroke - Major	243	Control	Hemorrhagic	Yes
Stroke - Major	173	Control	Unknown	No
Stroke - Major	0	Control	Unknown	No
Stroke - Major	10	TAVI	Ischemic	Yes
Stroke - Major	0	TAVI	Unknown	No
Stroke - Major	51	TAVI	Hemorrhagic	No
Stroke - Major	-12*	TAVI	Ischemic	No
Stroke - Major	3	TAVI	Unknown	No
Stroke - Major	120	TAVI	Hemorrhagic	No
Stroke - Major	0	TAVI	Unknown	No
Stroke - Major	136	TAVI	Hemorrhagic	Yes
Stroke - Major	39	TAVI	Hemorrhagic	Yes
Stroke - Major	151	TAVI	Ischemic	No
Stroke - Major	23	TAVI	Ischemic	No

Stroke - Major	2	TAVI	Hemorrhagic	No
Stroke - Major	1	TAVI	Unknown	No
Stroke - Major	0	TAVI	Unknown	Yes

+Time-to-event denotes time from implant date for TAVI patients and time from intention-to-treat randomization for standard therapy patients.

* Major stroke 12 days prior to TAVI.

Major stroke is defined as a persistent focal or global neurologic deficit associated with a modified Rankin Scale of ≥ 2.

TAVI transcatheter aortic valve implantation, TIA transient ischemic attack.

Table 6. Echocardiography Findings in the Study Population

	TAVI			Control		
			Hemodynamic Assessment			
Parameter	**Baseline**	**30 days**	**1 Year**	**Baseline**	**30 days**	**1 Year**
No. patients	166	144	88	164	120	51
AVA (cm^2)	0.6 ± 0.2	1.5 ± 0.4	1.6 ± 0.5	0.6 ± 0.2	0.8 ± 0.2	0.7 ± 0.3
Mean Gradient (mm Hg)	44.7 ± 15.4	11.4 ± 7.0	13.2 ± 11.2	43.2 ± 15.4	33.1 ± 12.6	44.3 ± 16.1
LVEF (%)	53.9 ± 13.1	57.9 ± 10.1	57.2 ± 10.6	51.2 ± 14.3	51.7 ± 13.9	56.9 ± 10.3
			Aortic Regurgitation			
Parameter	**Baseline**	**30 days**	**1 Year**	**Baseline**	**30 days**	**1 Year**
No. patients	173	153	98	174	125	52
Trans-valvular Aortic Regurgitation						
None	23 (13%)	47 (31%)	31 (32%)	20 (11%)	10 (8%)	4 (8%)
Trace/mild	114 (66%)	102 (67%)	61 (62%)	125 (72%)	93 (74%)	39 (75%)
Mod./severe	35 (20%)	2 (1%)	4 (4%)	23 (13%)	21 (17%)	9 (17%)
N/A	1 (1%)	2 (1%)	2 (2%)	6 (3%)	1 (1%)	0 (0%)
Para-valvular Aortic Regurgitation						
None	0 (0%)	22 (14%)	23 (23%)	0 (0%)	1 (1%)	1 (2%)
Trace/mild	0 (0%)	104 (68%)	58 (59%)	0 (0%)	2 (2%)	0 (0%)
Mod./severe	0 (0%)	18 (12%)	11 (11%)	0 (0%)	0 (0%)	0 (0%)
N/A	173 (100%)	9 (6%)	6 (6%)	174 (100%)	122 (98%)	51 (98%)
All Aortic Regurgitation						
None	23 (13%)	9 (6%)	11 (11%)	20 (11%)	8 (6%)	4 (8%)
Trace/mild	114 (66%)	119 (78%)	70 (71%)	125 (72%)	95 (76%)	39 (75%)
Mod./severe	35 (20%)	23 (15%)	15 (15%)	23 (13%)	21 (17%)	9 (17%)

N/A	1 (1%)	2 (1%)	2 (2%)	6 (3%)	1 (1%)	0 (0%)

AR denotes aortic regurgitation, AVA aortic valve area, LVEF left ventricular ejection fraction, mod moderate, TAVI transcatheter aortic valve implantation.

Table 7: PARTNER Study – Participating Study Sites and Key Personnel

Barnes Jewish Hospital, St. Louis, MO	Principal investigators: J. Lasala, R. Damiano; co-investigators: A. Zajarias, H. Maniar; site coordinators: K. Striler, J. Zoole
Brigham & Women's Hospital, Boston, MA	Principal investigators: A. Eisenhauer, M. Davidson; co-investigator: F. Welt; site coordinator: T. Charleson; anesthesiology/echocardiography: W. Gross
Cedars-Sinai Medical Center, Los Angeles, CA	Principal investigators: R. Makkar, G. Fontana; co-investigators: A. Trento, S. Kar; site coordinators: M. Gheorghiu, A Doumanian; echocardiography: K. Tolstrup, R. Siegel
Cleveland Clinic Foundation, Cleveland, OH	Principal investigators: M. Tuzcu, L. Svensson; co-investigators: S. Kapadia, E. Roselli; site coordinators: R. Bartow, C. Gerace; echocardiography: L. Rodriguez, W. Stewart, R. Grim; anesthesiology/echocardiography: R. Savage
Columbia University Medical Center, New York, NY	Principal investigators: M. Leon, C. Smith; co-investigators: J. Moses, S. Kodali, M. Williams; site coordinators: M. Hawkey, S. Schnell; echocardiography: R. Hahn, L. Gillam
Cornell University, New York, NY	Principal investigators: S. Chiu Wong, K. Krieger; co-investigators: G. Bergman, A. Salemi; site coordinator: D. Reynolds; echocardiography: R. Devereux.
Emory University Hospital, Atlanta, GA	Principal investigators: P. Block, R. Guyton; co-investigators: V. Babaliaros, V. Tjhourani; site coordinators: E. Block, E. Tequia; echocardiography: S. Howell

Herzzentrum Leipzig, Leipzig, Germany	Principal investigators : F. Mohr, G. Schuler; co-investigator: T. Walther; site coordinator: S. Ott
Intermountain Medical Center, Murray ,UT	Principal investigators: B. Whisenant, K. Jones; co-investigators: S. Clayson, J. Revenaugh; site coordinators: B. Miller, J. Flores
Laval Hospital, Quebec, Canada	Principal investigators: J. Rodes-Cabau, D. Doyle; co-investigator: Dumont; site coordinator: J. Aube
Massachusetts General Hospital, Boston, MA	Principal investigators: I. Palacios, G. Vlahakes; co-investigators: A. Agnihotri, I. Inglessis; site coordinator: M. Daher; echocardiography:A. Jonri
Mayo Clinic, Rochester, MN	Principal investigators: D. Holmes, T. Sundt; co-investigators: C. Rihal K. Greason; site coordinators: B. Anderson, D. Rolbiecki; echocardiography: H. Michelena, M. Sarano, K. Andrew
Medical City Dallas, Dallas, TX	Principal investigators: M. Mack, D. Brown; co-investigators: B. Bowers, T. Dewey; site coordinators: C. McKibben, A. Kenady; echocardiography: D. Gopal
Northshore University Health System, Evanston, IL	Principal investigators: T. Feldman, J. Alexander; co-investigator: M. Salinger; site coordinators: D. Seifert, C. Focks; echocardiography: S. Smart; anesthesiology/echocardiography: J. Marymount
Northwestern Medical Center, Chicago, IL	Principal investigators: C. Davidson, P. McCarthy; co-investigators: N. Beohar, C. Malaisrie; site coordinators: K. Madden, M. DeAngelis; echocardiography: I. Mikati

Ochsner Clinic, New Orleans, LA	Principal investigators: S. Ramee, G. Parrino; co-investigators: T. Collins, M. Bates; site coordinator: B. Hirstius; echocardiography: L. Bienvenu
Scripps Clinic, La Jolla, CA	Principal investigators: P. Teirstein, S. Brewster; co-investigators: J. Tyner; site coordinators: S. Clarke, T. Buchanan, E. Anderson
Stanford University Medical Center, Palo Alto, CA	Principal investigators: C. Miller, A. Yeung; co-investigators: W. Fearon, M. Fischbein; site coordinators: M. Speight, C. McWard; echocardiography: D. Liang
St. Luke's Medical Center, Kansas City, MO	Principal investigators: D. Cohen, K. Allen; co-investigator: A. Grantham; site coordinators: J. Hall, M. Miller
St. Paul's Hospital, Vancouver, Canada	Principal investigators: J. Webb, A. Cheung; co-investigators: J. Ye, S. Lichtenstein; site coordinator: E. Zwanenburg
Toronto General Hospital, Toronto, Canada	Principal investigators: E. Horlick, C. Feindel
University of Miami, Miami, FL	Principal investigators: W. O'Neill, D. Williams ; co-investigators: A. Heldman, A. Medina; site coordinator: S. Morales; echocardiography: M. Bilsker
University of Pennsylvania, Philadelphia, PA	Principal investigators: J. Bavaria, H.C. Herrmann; co-investigator: W. Szeto; site coordinators: L. Roche, L. Walsh
University of Washington, Seattle, WA	Principal investigators: M. Riesman, E. Verrier; co-investigators: G. Aldea, L. Dean; site coordinator: R. Letterer; echocardiography: C. Otto

Washington Hospital Center, Washington, DC	Principal investigators: G. Pichard, P. Corso; co-investigators: S. Boyce, L. Satler; site coordinator: P. Okubagzi; echocardiography: F. Asch, S. Goldstein

Figure Legends

Figure 1. The Edwards-SAPIEN^{TM} Heart Valve

The integrated Edwards-SAPIEN^{TM} heart valve system for TAVI consists of a balloon-expandable bovine pericardial tri-leaflet valve affixed to a stainless steel, tubular, slotted support structure (Panel A), which is tightly compressed immediately prior to deployment onto a balloon catheter. The compressed device is inserted into a tip-deflecting catheter delivery system. After advancement in the aorta and placement of the device just below the native aortic valve, the balloon is inflated which expands the valve and support frame (Panel B). The newly functioning bioprosthetic valve is permanently secured to the underlying native valve leaflets and the aortic annulus.

Figure 1, Video 1. Cine-fluoroscopy of valve deployment during rapid right ventricular pacing. The crimped valve and support frame is expanded with underlying balloon inflation. Also seen are the trans-esophageal echocardiography probe and the temporary right ventricular pacing lead.

Figure 1, Video 2. Animation of the complete trans-femoral TAVI procedure, including femoral artery sheath insertion, retrograde balloon aortic valvuloplasty, advancement of the TAVI system across the aortic valve, and subsequent deployment of the valve and support frame.

Figure 2. Overall PARTNER Trial Design

A total of 3,105 patients with AS and symptoms were screened at the investigator sites for enrollment eligibility. Major reasons for exclusion in the trial included (1) AS severity did not fulfill entry criteria, (2) other anatomic exclusions (e.g. annulus size too large, LV function too low, MR >3+), (3) risk profile (including STS score) too low, (4) risk profile too high, such that meaningful treatment benefit or one year survival not likely, and (5) patient refuses randomization. Post-screening eligibility was further adjudicated during a web-based conference call, in which every case was reviewed by executive committee members including relevant imaging studies. After final approval by the executive committee, patients were permitted to be randomized into either the high surgical risk or inoperable cohorts. Prior to

randomization into the inoperable cohort, trans-femoral access was assessed and subjects without suitable anatomy were excluded from the study. Overall, 34% of the total number of screened AS patients were ultimately randomized in the PARTNER trial. This manuscript reports the results only from the inoperable patient cohort, comprising 12% of the screened AS patients.

Figure 3. Study Flow for the Inoperable Patients in the PARTNER Trial

Subject status at 30 days and 1 year among patients randomly assigned to TAVI or standard medical therapy (control) is provided. The term "followed" means that the survival and rehospitalization endpoint information is available for the designated time points. The proportion followed was 99.4% at 30 days and 94.4% at 1 year for the control group, and 100% at 30 days and 100% at 1 year for the TAVI group. Except for the 5 withdrawals in control patients, complete survival information is available for all patients, as of the analysis close date (March 16, 2010, median follow-up = 1.6 years). TAVI denotes transcatheter aortic valve implantation.

Figure 1. The Edwards-SAPIEN^{TM} Heart Valve

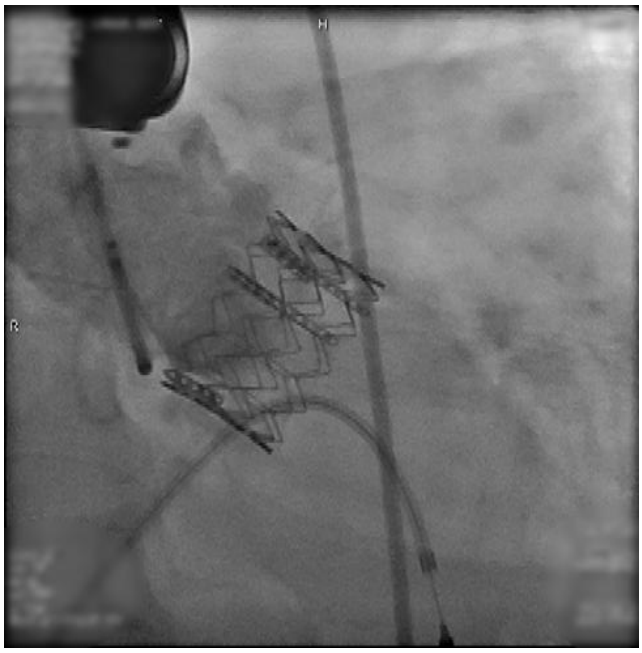
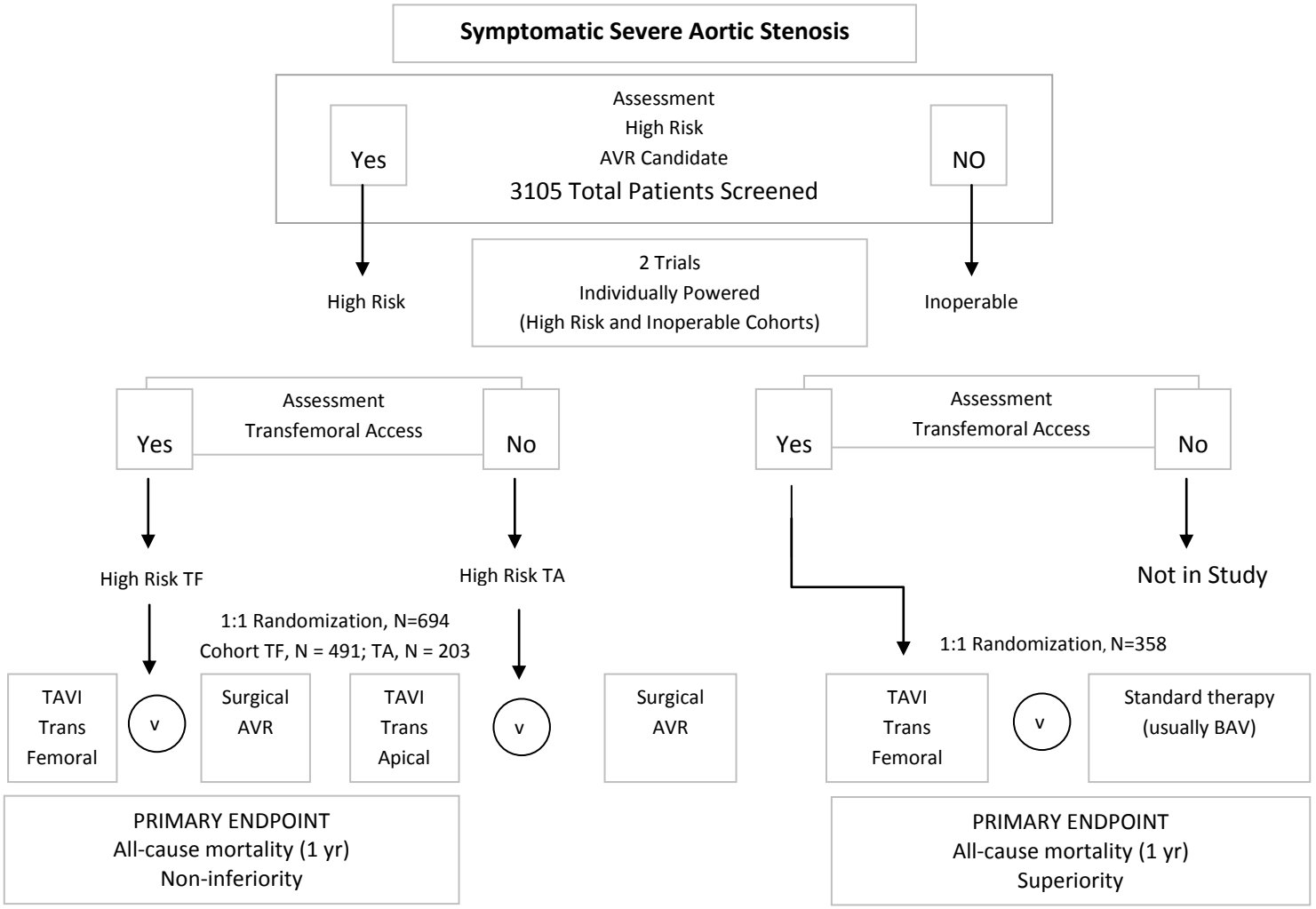
A	B
	

Figure 2. Overall PARTNER Trial Design



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