Online appendix

**Primary endpoints:**

Device success: Stable device placement and adequate function as assessed by angiography and echocardiography immediately post-procedure.

Major adverse cardiac and cerebrovascular events (MACCE): A composite of any death, myocardial infarction, or disabling stroke at 30 days post-procedure.

**Secondary endpoints**

Acute procedural success: Device success and the absence of periprocedural MACCEs at post-operative day (POD) 1.

30 days major adverse events (MAE): Any of the following adverse events: death, myocardial infarction, disabling stroke, repeat aortic valve procedure, cardiogenic shock, or endocarditis at 30 days.

6 months MAE: Any of the following adverse events: death, disabling stroke, repeat aortic valve procedure or endocarditis at 6 months.

Survival: Freedom from death at 1 year.
Functional improvement: Functional improvement from baseline per New York Heart Association (NYHA) functional classification at 30 days, 6 months and 1 year.

Hemodynamic valve performance: Peak pressure gradient, mean pressure gradient and derived calculated measures of prosthetic valve function, as well as aortic regurgitation.

Follow-up: 30 days, 6 months and annually thereafter for 5 years.

**Inclusion Criteria:**

1. Patient understands the implications of participating in the study and provides informed consent
2. Patient is willing to comply with specified follow-up evaluation and can be contacted by telephone
3. Age ≥75 years
4. Severe, aortic stenosis (echocardiographically derived mean gradient > 40 mm Hg, and/or jet velocity > 4 m/s, or an initial aortic valve area of < 0.8 cm^2)
5. Symptoms related to the aortic valve disease, as demonstrated by NYHA Functional Class II or greater
6. EuroSCORE scale of ≥9 points indicating a predicted risk for mortality of >11% according to the logistic EuroSCORE

7. Echocardiographically determined anteroposterior aortic annulus diameter of >19 and <23 mm

8. Echocardiographically determined sinotubular junction diameter of ≥23 mm

Exclusion Criteria:

1. Congenital unicuspid or bicuspid aortic valve

2. Fused commissures

3. Severe eccentricity of calcification

4. Echocardiographic evidence of intracardiac mass, thrombus, or vegetation.

5. Severe left ventricular dysfunction (LVEF < 25%)

6. More than mild right ventricular dysfunction

7. Hypertrophic obstructive cardiomyopathy

8. Moribund patients, or patients with a noncardiac disease limiting by itself life expectancy to less than 12 months

9. Known hypersensitivity or contraindication to any study medication

10. Known sensitivity to contrast medium that cannot be adequately controlled with pre-medication

11. Known allergy or sensitivity to Nitinol

12. Sepsis, or acute endocarditis
13. Blood dyscrasia such as acute anemia, leucopenia, or thrombocytopenia; bleeding diathesis, or coagulopathy.

14. Renal insufficiency and/or end stage renal disease requiring chronic dialysis

15. Liver disease as indicated by jaundice, ascites, ALT/AST > 3 x UNL, elevation of total bilirubin > 1.5 mg/dl, albumin < 3.0 g/l, or INR > 1.5 (if not on anticoagulation).

16. Significant lung disease (e.g. FEV1 < 1.2L or FEV1 < 50%).

17. Active peptic ulcer or GI bleeding within 3 months from the planned index procedure

18. Untreated clinically significant coronary artery disease requiring revascularisation

19. Cardiogenic shock, suspected cardiogenic shock, or hemodynamic instability requiring inotrop support or mechanical heart assistance

20. Peripheral vascular disease, including abdominal and thoracic aortic disease, which could pose a problem for eventual transarterial mechanical support (e.g. Intraaortic Balloon Pump)

21. Need for emergency surgery, cardiac or noncardiac

22. History of myocardial infarction in the last 6 weeks.

23. History of TIA or stroke in the last 6 months.
24. Any therapeutic invasive cardiac procedure, except aortic balloon valvuloplasty, performed within 30 days from the planned index procedure, or 6 months, in case of implantation of drug-eluting stents.

25. Uncontrolled atrial fibrillation

26. Pre-existing aortic valve replacement

27. Severe (greater than 3+) mitral regurgitation

28. Severe (greater than 3+) aortic regurgitation

29. Patient is currently enrolled in another investigational device or drug trial