Valve Trialist. What is going on? Focused Update European Registry

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Real-World Use of a Repositionable Self-Expanding Transcatheter Aortic Valve: Primary Results of the Evolut R FORWARD Study

Evolut R FORWARD Study
Background

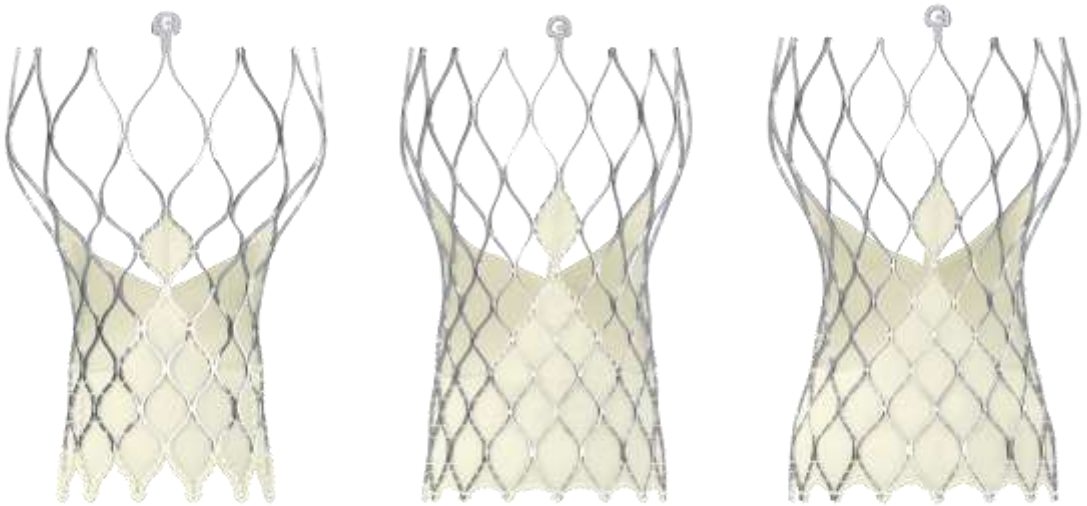
- Transcatheter aortic valve implantation (TAVI) is now standard of care at specialized heart centers for patients with symptomatic aortic stenosis at increased surgical risk.
- Iterative new TAVI valves are becoming commercially available following evaluation in small study cohorts.
  - The next generation Evolut R TAV demonstrated 2.5% 30-day mortality in 241 high-risk patients in the Evolut R US Study.[1]
- Clinical outcomes using next generation TAVs in large patient populations from real-world clinical practice are an important addition to the TAVI literature.

[1]Popma JJ, et al. JACC Cardiovasc Interv 2017; 10: 268-75.

Evolut R FORWARD Study
Evolut R System

Catheter Delivery System

14Fr-equivalent profile



Transcatheter Valve (23, 26, 29 mm)

Supra-annular design, excellent hemodynamics

The Evolut R TAV is a supra-annular porcine valve in a self-expanding Nitinol frame that can be resheathed or fully recaptured to assist with accurate valve positioning.

Evolut R FORWARD Study
Overview

OBJECTIVE	To assess the safety and clinical performance of the CoreValve Evolut R System in patients with symptomatic native aortic stenosis or failed bioprothesis in routine practice
DESIGN	Prospective, single arm, multicentre, observational study
PATIENTS	STS predicted risk of mortality ≥8% **OR** Heart Team agreement of increased surgical risk due to frailty or comorbidities.
ENDPOINTS	**Safety**: All-cause mortality and all stroke at 30 days **Clinical Performance**: Valve hemodynamics at discharge
CORE LAB	Echocardiography (Mayo Clinic, Rochester, MN, USA)
OVERSIGHT	100% monitoring of patient consent and endpoint-related events 99.0% for 30-day follow-up

Evolut R FORWARD Study

Study oversight and participation

Steering Committee Members

*Eberhard Grube, *University of Bonn*

*Stephan Windecker, *Inselspital/Universitätsspital Bern*

Sabine Bleiziffer, *Deutsches Herzzentrum München*

Johan Bosmans, *UZ Antwerp*

Ganesh Manoharan, *Royal Victoria Hospital Belfast*

Thomas Modine, *CHRU de Lille*

Nicolas Van Mieghem, *Erasmus MC Rotterdam*

Echocardiographic Core Lab

Jae K. Oh, MD, Mayo Clinic, Rochester, MN, USA

Clinical Events Committee

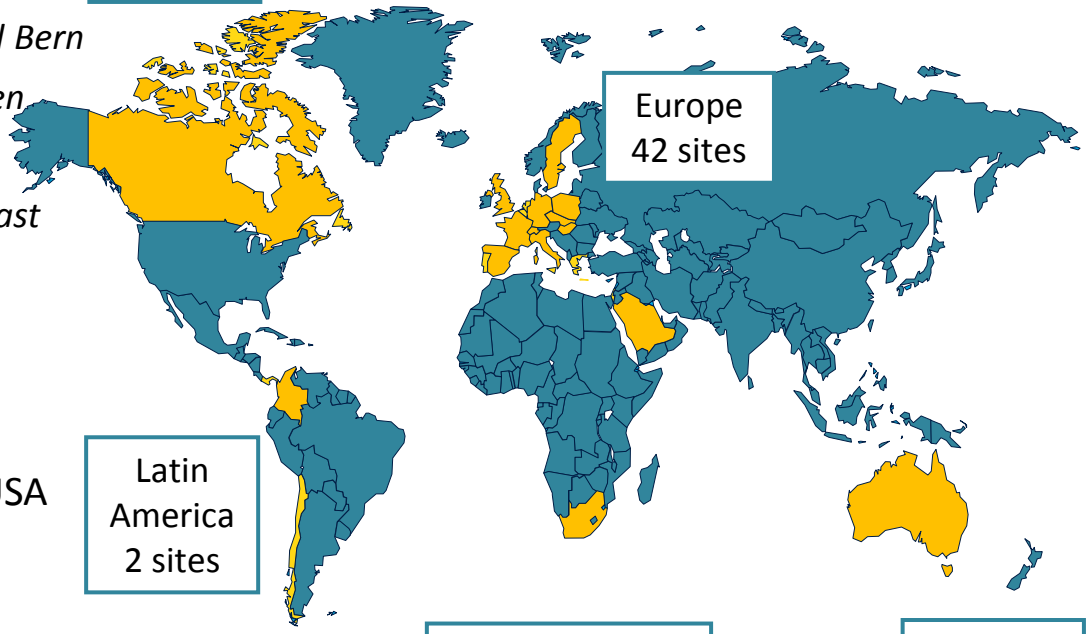
Baim Institute for Clinical Research, Boston, MA, USA

Sponsor

Medtronic

*Co-principal Investigators

53 sites in 20 countries



Evolut R FORWARD Study

Inclusion and exclusion criteria

INCLUSION

- Symptomatic native aortic valve stenosis or surgical bioprosthetic valve failure
- Acceptable candidate for **elective** treatment with the Evolut R System in conformity with the local regulatory context
- Age ≥80 years **OR** considered to be at high or greater risk for surgical aortic valve replacement (AVR) where high risk is defined as:
  - STS predicted risk of mortality ≥8%

    OR
  - Heart team agreement of risk for AVR due to frailty or comorbidities.

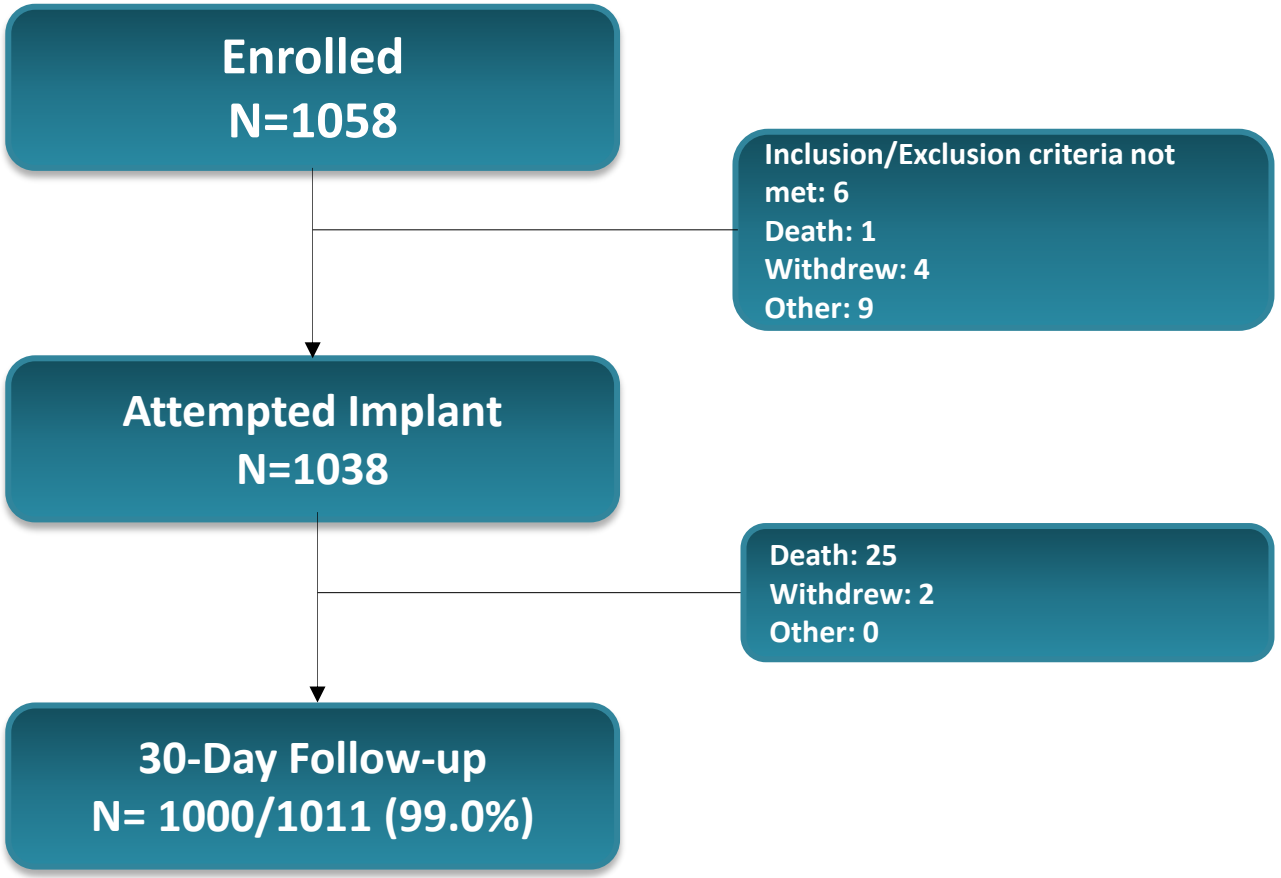
EXCLUSION

- Contraindication to aspirin, heparin, bivalirudin, ticlopidine, clopidogrel, Nitinol, contrast media
- Mechanical heart valve in aortic position
- Sepsis, including active endocarditis
- Anatomically unsuitable for the Evolut R system
- Estimated life expectancy <1 year
- Participating in another trial that may influence the outcome of this trial
- Need for emergency surgery for any reason

Evolut R FORWARD Study
Study methods

- Enrolment controlled for centre or country bias
  - Maximum from any 1 centre of 7.5% and from any 1 country of 40% of total enrolment
- Multi-slice CT of the peripheral vasculature and aortic annulus required
- Standard hospital practice techniques at implant and during follow-up
- Recommended follow-up at discharge, 30 days, and annually through 3 years per standard practice
- Modified Rankin Score (mRS) at baseline and at each follow-up by certified assessor
  - Performed at 90 days after suspected neurological event
- Independent Clinical Events Committee adjudicated safety endpoints per VARC-2.

Evolut R FORWARD Study
Patient flow



Evolut R FORWARD Study
Baseline characteristics

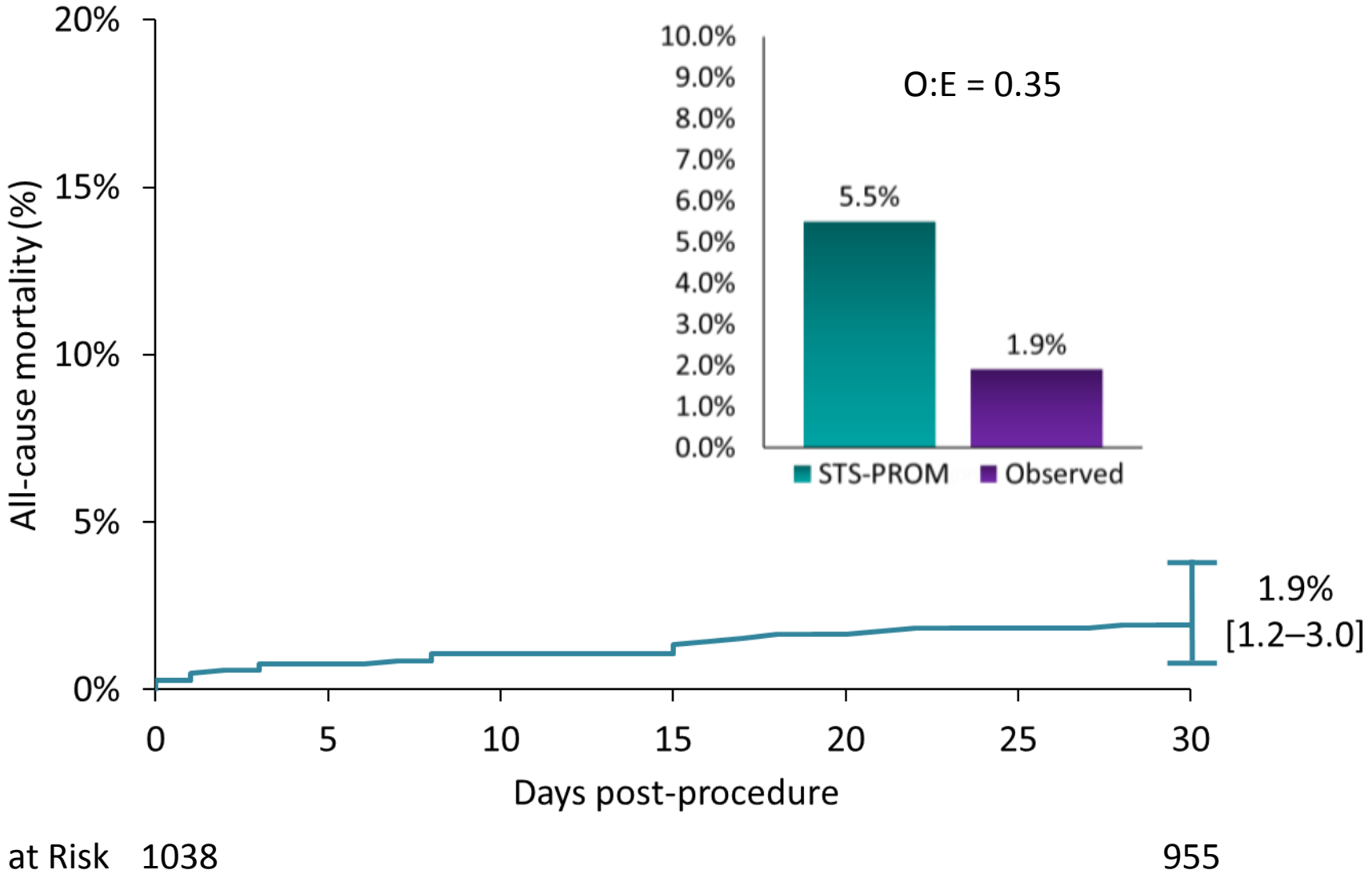
Mean ± standard deviation or %	Evolut R N=1038
Age (years)	81.8 ± 6.2
Female	64.9
Society of Thoracic Surgeons Predicted Risk of Mortality (%)	5.5 ± 4.5
EuroSCORE II (%)	5.7 ± 5.0
New York Heart Association class III/IV	72.0
Diabetes	29.9
Serum creatinine >2 mg/dL	5.6
Chronic lung disease/chronic obstructive pulmonary disease	26.4
Frailty	33.9
Assisted living	15.4
Pacemaker or implanted cardioverter defibrillator	11.9

Evolut R FORWARD Study
Procedural characteristics

Mean ± standard deviation or %	Evolut R N=1038
Local anaesthesia	65.0
Iliofemoral access route	98.0
Implanted valve size	
23 mm	6.1
26 mm	36.6
29 mm	57.3
Pre-TAVI balloon dilation performed	45.5
Post-implant dilation performed	33.1
Patients with resheathing or recapture performed	25.8
EnVeo R* InLine sheath used	88.7
Multiple valves (≥ 2 implanted)	1.0

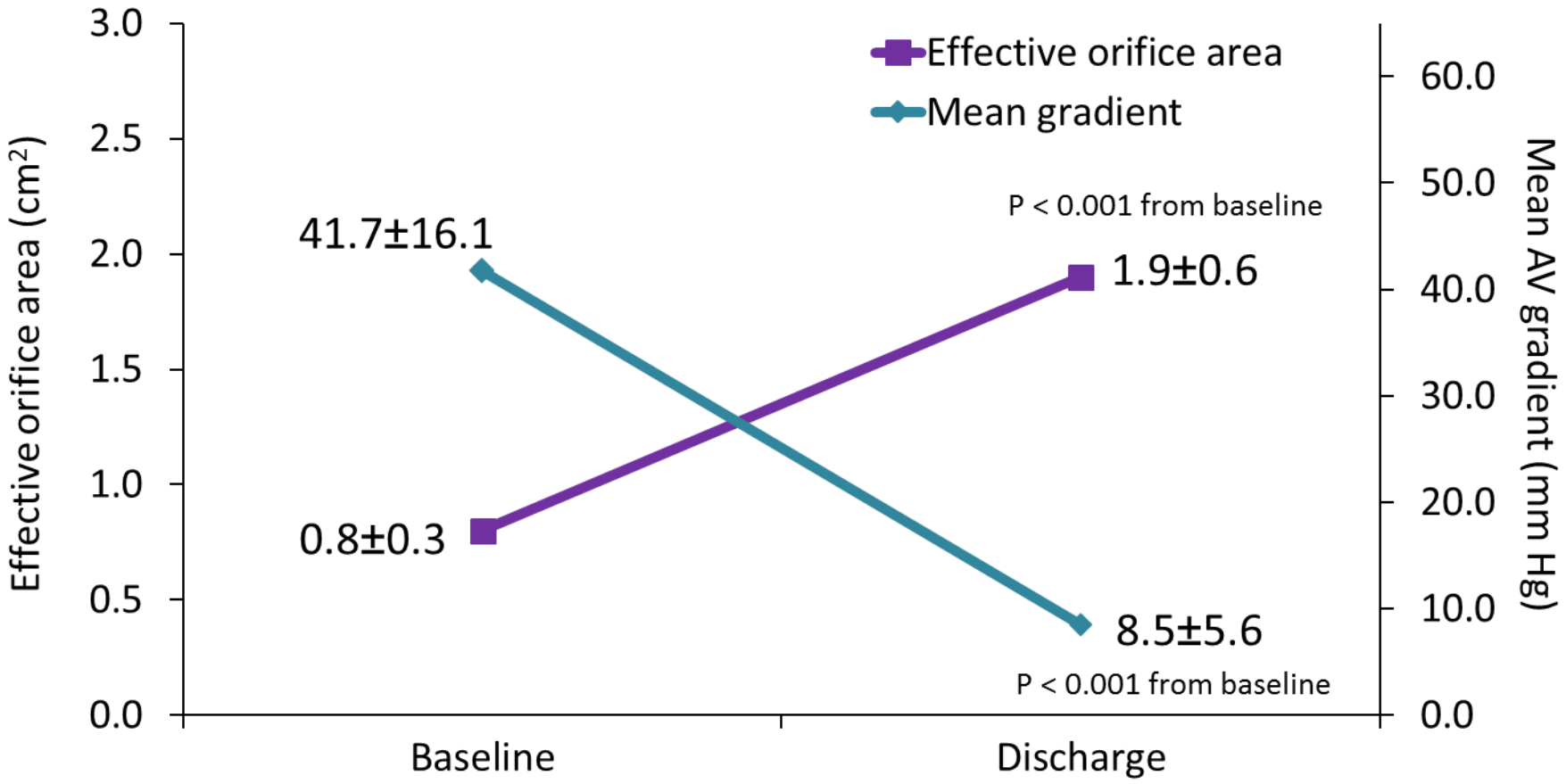
*Medtronic.

Evolut R FORWARD Study
Primary endpoint



No. at Risk 1038 955

Evolut R FORWARD Study
Hemodynamics at discharge

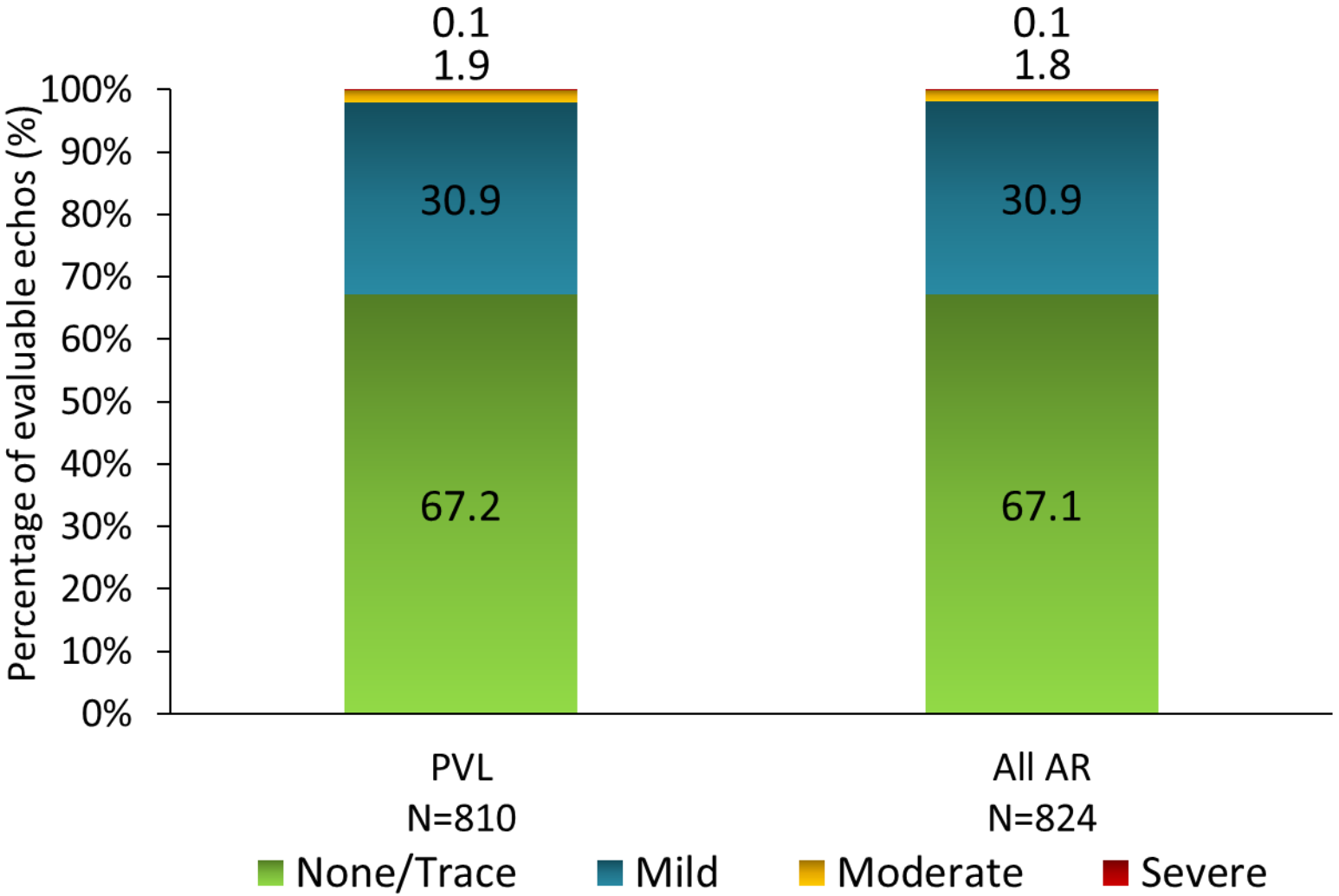


Gradient	913	866
Effective orifice area	626	541

Per independent core laboratory assessment.

Evolut R FORWARD Study

Valve regurgitation at discharge



Per independent core laboratory assessment.

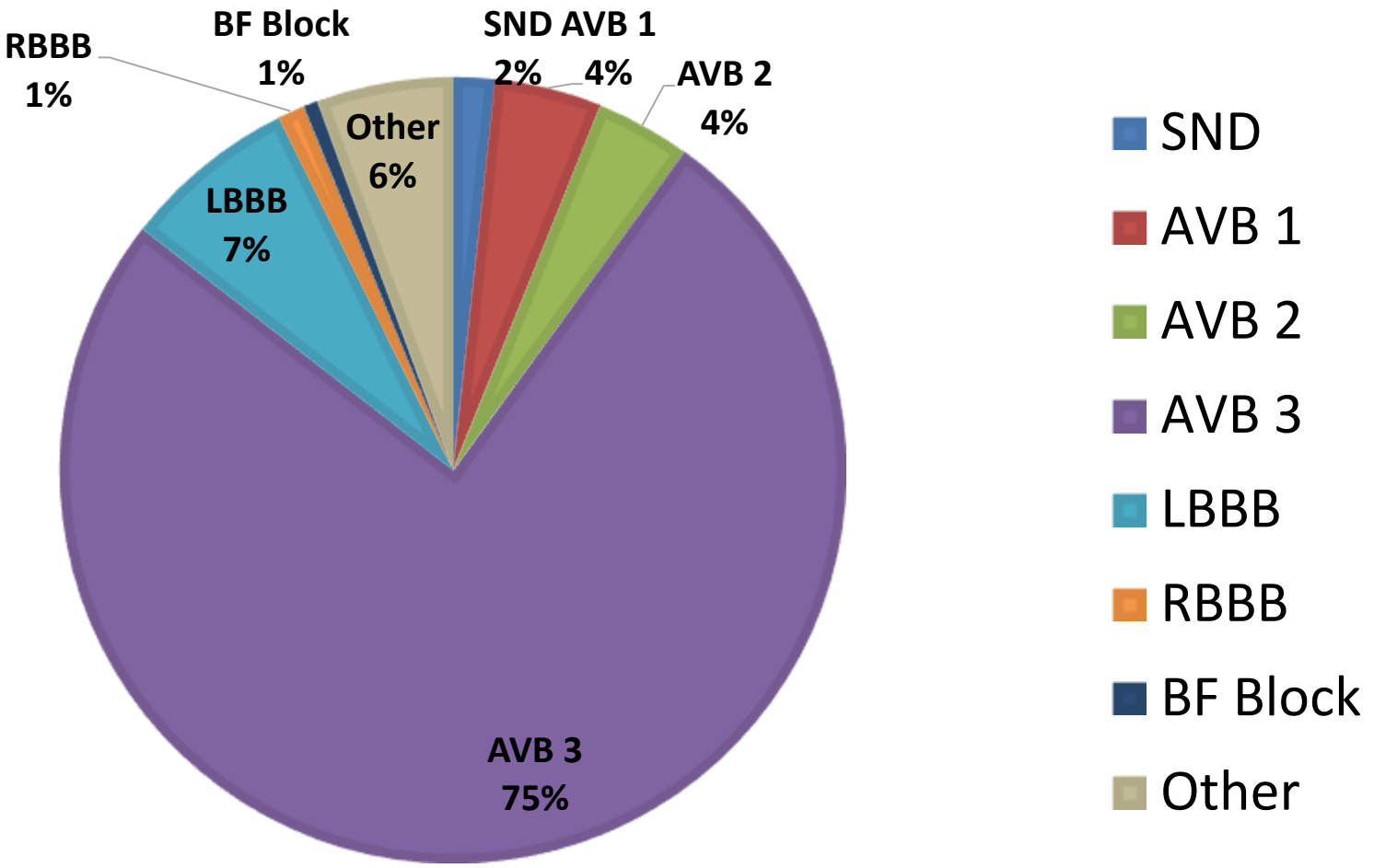
Evolut R FORWARD Study
Safety outcomes at 30 days

No. (Kaplan-Meier rates as %)	Evolut R N=1038
All-cause mortality	20 (1.9)
All Stroke	29 (2.8)
Disabling stroke	18 (1.8)
Major vascular complication	67 (6.5)
Life-threatening or disabling bleeding	34 (3.3)
Prosthetic valve thrombosis	0 (0.0)
Valve embolization*	7 (0.7)
Valve migration	2 (0.2)
Pacemaker	180 (17.5)
Coronary obstruction	0 (0.0)
Annular rupture	0 (0.0)

*Per VARC-2 (Pop-outs).

Evolut R FORWARD Study

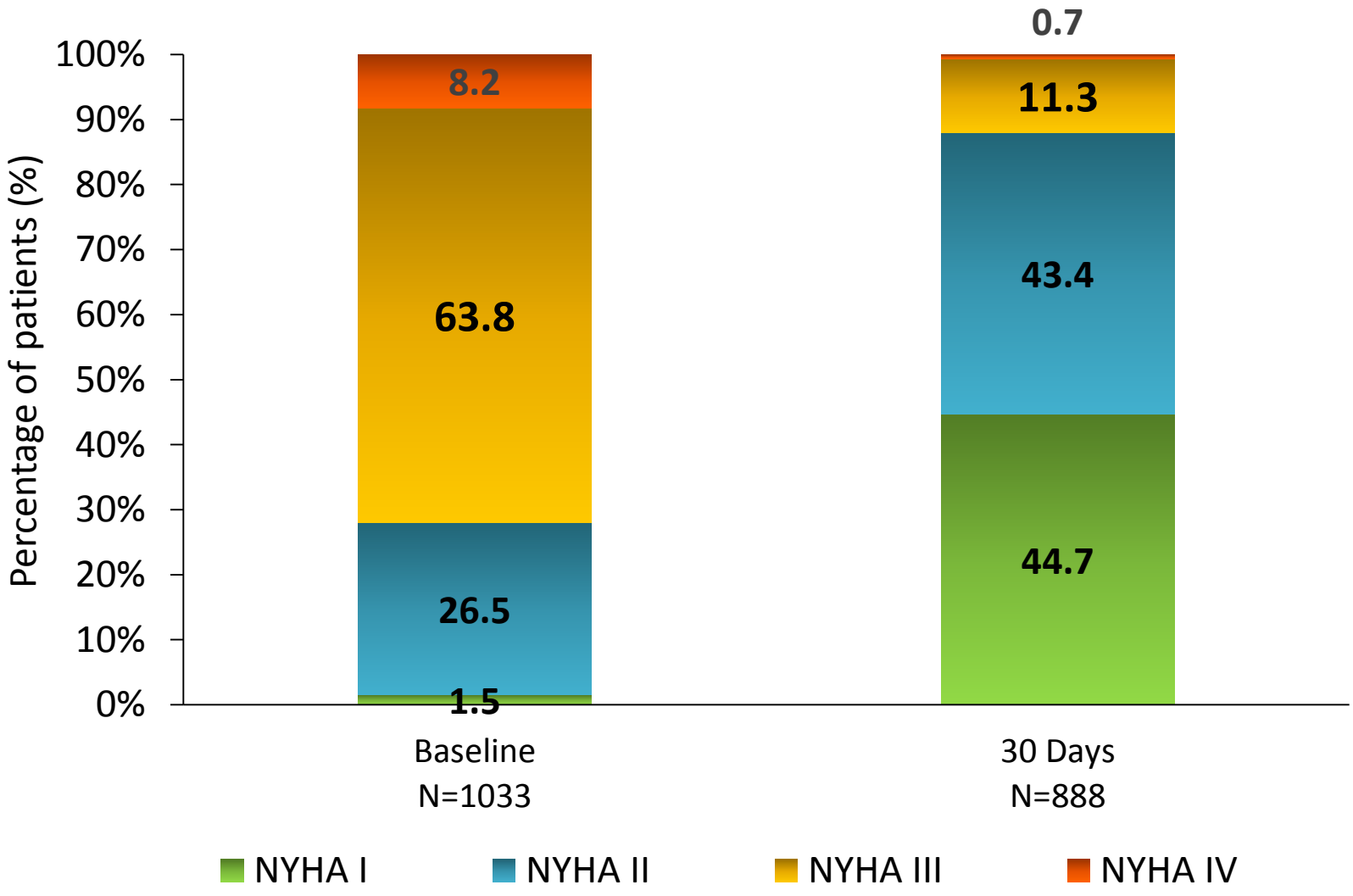
Reasons for pacemaker within 30 days



AVB = atrioventricular block; BF = bifascular; LBBB = left bundle branch block; RBBB = right bundle branch block; SND; sinus node dysfunction

Evolut R FORWARD Study

NYHA functional class



Evolut R FORWARD Study
Early outcomes by repositioning

Kaplan-Meier rates as %	Repositioned N=265*	Non-Repositioned N=763*	P Value†
All-cause mortality	1.9	1.8	0.96
All stroke	2.7	2.9	0.83
Disabling stroke	2.3	1.6	0.47
Major vascular complication	6.4	6.0	0.82
Life-threatening or disabling bleeding	1.5	3.4	0.11
Prosthetic valve thrombosis	0.0	0.0	NA
Valve embolization‡	1.1	0.5	0.30
Valve migration‡	0.8	0.0	0.02
Pacemaker	19.3	16.9	0.34

*10 patients without repositioning information. †P value comparing patients in whom resheathing or recapturing was performed. ‡Valve Academic Research Consortium-2. NA = not analyzable.

Evolut R FORWARD Study
Summary

At 30 days post-TAVI the Evolut R FORWARD Study demonstrated excellent, reproducible results in real world clinical practice:

- Low mortality of 1.9%
- Low stroke rates of 2.8% – not affected by repositioning
- Repositioning was attempted in 25.8% of patients
- 98.1% of patients with ≤ mild regurgitation
- 98.9% of patients with 1 valve in proper anatomical position
- No coronary obstruction or annular rupture
- Excellent hemodynamics

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Clinical Outcomes With a Repositionable Self-Expanding Transcatheter Aortic Valve Prosthesis

The International FORWARD Study

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ABSTRACT

BACKGROUND Clinical outcomes in large patient populations from real-world clinical practice with a next-generation self-expanding transcatheter aortic valve are lacking.

OBJECTIVES This study sought to document the clinical and device performance outcomes of transcatheter aortic valve replacement (TAVR) with a next-generation, self-expanding transcatheter heart valve (THV) system in patients with severe symptomatic aortic stenosis (AS) in routine clinical practice.

METHODS The FORWARD (CoreValve Evolut R FORWARD) study is a prospective, single-arm, multinational, multicenter, observational study. An independent clinical events committee adjudicated safety endpoints based on Valve Academic Research Consortium-2 definitions. An independent echocardiographic core laboratory evaluated all echocardiograms. From January 2016 to December 2016, TAVR with the next-generation self-expanding THV was attempted in

FORWARD Study results published in JACC (August 15, 2017)!

CONCLUSIONS TAVR using the next-generation THV is clinically safe and effective for treating older patients with severe AS at increased operative risk. (CoreValve Evolut R FORWARD Study [FORWARD]; NCT02592369)
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Thank You	Ευχαριστώ
Merci	תודה
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Grazie	Gracias
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Děkuji	Köszönöm