Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) – Long Term Outcomes

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National Principal Investigators, on behalf of the MOMENTUM 3 Investigators

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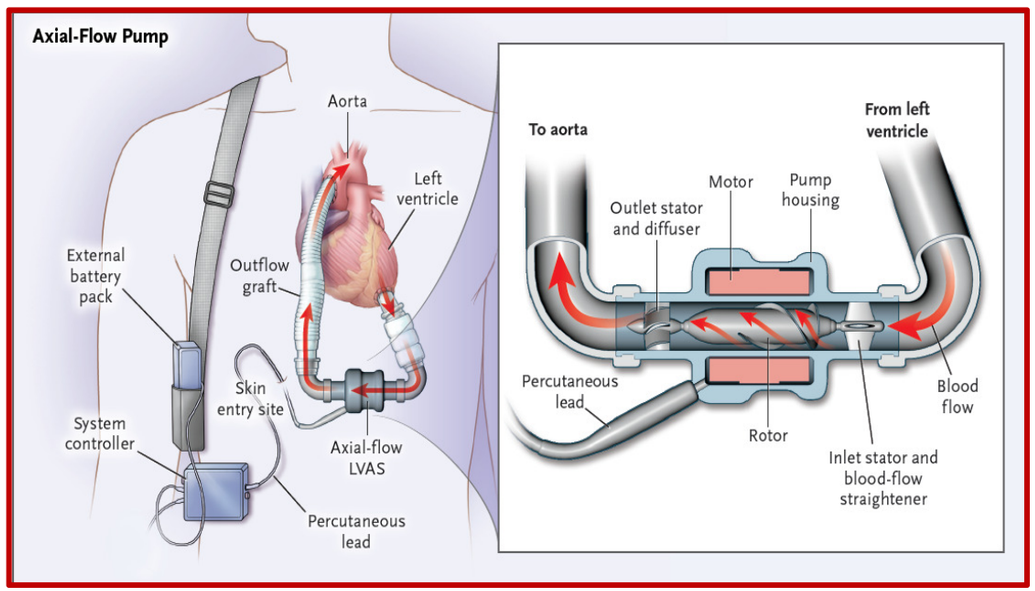
Background

- **Continuous-flow Left Ventricular Assist Systems (LVAS) improve survival and quality of life in patients with advanced heart failure refractory to medical therapy[1]**



The HeartMate II LVAS is a mechanical bearing axial continuous-flow blood pump;
An LVAS approved for *both* Bridge-To-Transplant (BTT) and Destination Therapy (DT) patients

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[1]Slaughter et al. Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device. *N Engl J Med.* 2009;361(23):2241-2251.

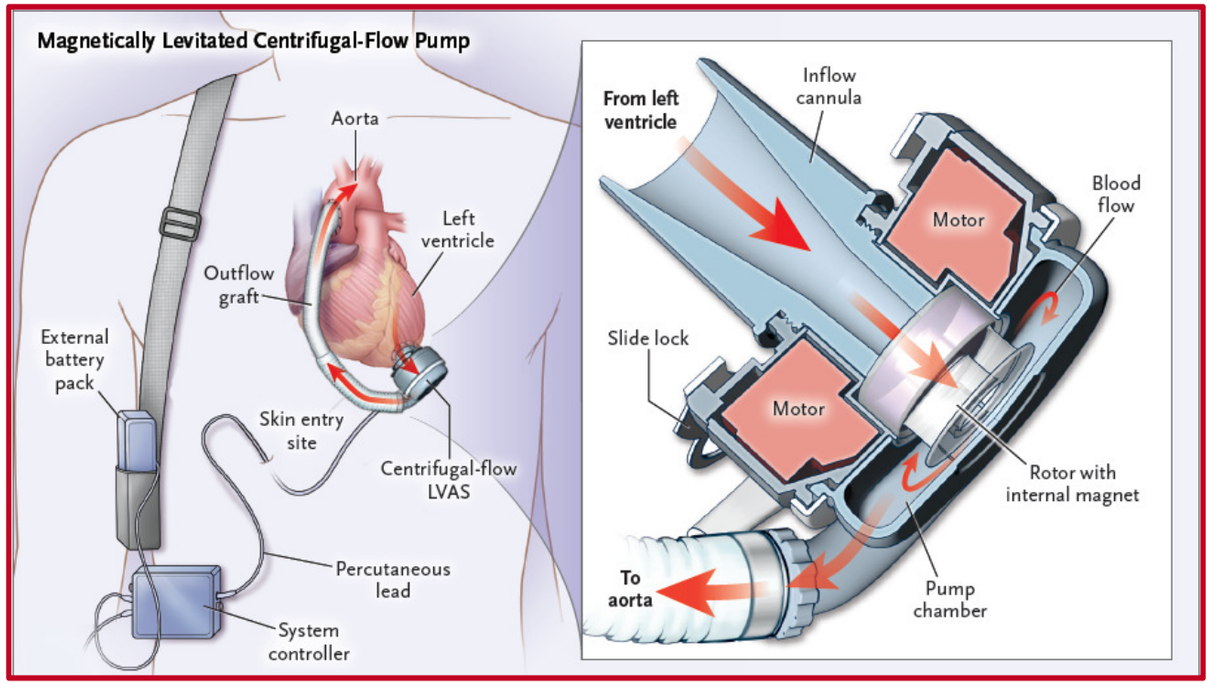
Background

- LVAS, such as the HeartMate II, are associated with significant risk of pump thrombosis requiring pump exchange, limiting long-term durability

- Other major adverse events of concern with LVAS devices include stroke, bleeding and device related infection[1]

[1]Slaughter et al. Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device. *N Engl J Med.* 2009;361(23):2241-2251.

HeartMate 3 LVAS



- **Wide** blood-flow passages to reduce shear stress
- **Frictionless** with absence of mechanical bearings
- **Intrinsic Pulse** designed to reduce stasis and avert thrombosis

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Mehra et al. A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure. *N Engl J Med* 2017;376(5):440-50.
Bourque et al. Design Rationale and Preclinical Evaluation of the HeartMate 3 Left Ventricular Assist System for Hemocompatibility. *ASAIO J* 2016;62(4):375-83

MOMENTUM 3 Target Population

- **Patients with advanced heart failure and severe limitations (NYHA IIIB or IV), refractory to guideline-mandated medical management** and *deemed as necessary candidates for left ventricular assist device implantation*, irrespective of the intended goal of pump support (BTT or DT)

- **Key exclusion criteria** included planned biventricular support, irreversible end-organ dysfunction, or active infection

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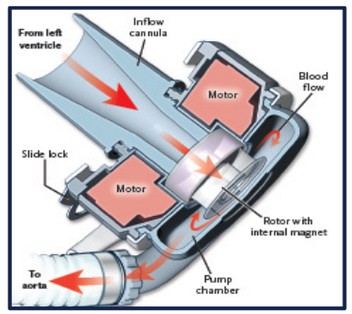
Heatley et al. Clinical trial design and rationale of the Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3 (MOMENTUM 3) investigational device exemption clinical study protocol. *J Heart Lung Transplant.* 2016;35(4):528-36.

Study Design



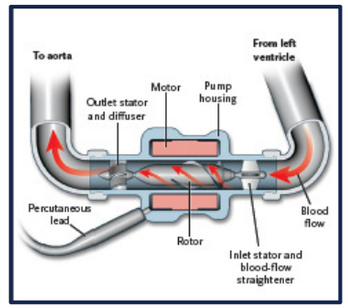
Patient meets MOMENTUM 3 eligibility criteria?

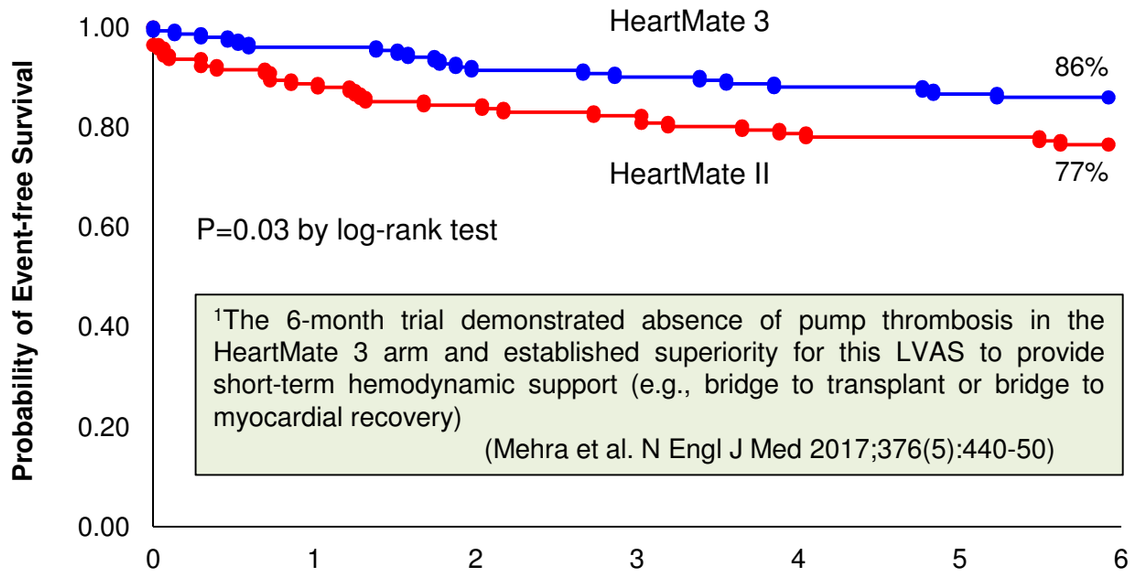
↓

Randomization 1:1

↓

Short Term (ST) Cohort[1]
N=294
6-month follow-up





[1]The 6-month trial demonstrated absence of pump thrombosis in the HeartMate 3 arm and established superiority for this LVAS to provide short-term hemodynamic support (e.g., bridge to transplant or bridge to myocardial recovery)

(Mehra et al. N Engl J Med 2017;376(5):440-50)

No. at Risk							
HeartMate 3	152	146	138	135	130	128	127
HeartMate II	142	125	119	116	110	106	103

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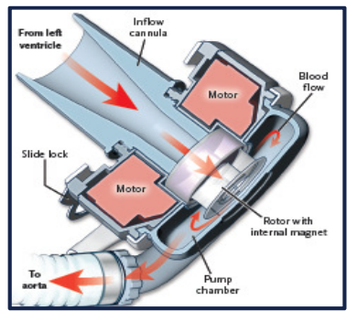
Study Design



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Short Term (ST) Cohort[1]
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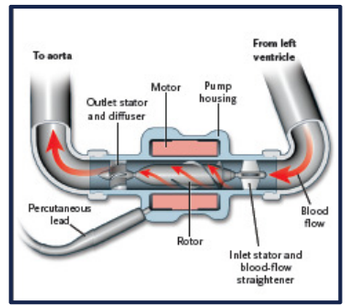

Additional 72 patients enrolled

Long Term (LT) Cohort
N=366
2-year follow-up

Full Cohort
N=1028
2-year follow-up

Intent-to-Treat (ITT) Population
N=366

HeartMate 3 Pump
N=190

HeartMate II Pump
N=176

Withdrawn before implant
N = 4
No LVAD implant: 1
Withdrawal of consent: 1
Transplant: 1
Implanted with non-study LVAD: 1

Withdrawn before implant
N = 1
Death: 1

Per Protocol Population
N=361

Implanted with HeartMate 3
N=189

Implanted with HeartMate II
N=172

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[1]Mehra et al. A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure. *N Engl J Med* 2017;376(5):440-50.

Study Aim and Primary Endpoint

Study Aim

- **The long-term (2-year) study** is designed to ascertain success to optimally support patients who wait for extended periods for heart transplantation or are ineligible for heart transplantation (e.g., destination therapy)

Primary Endpoint

- **Survival at 2 years free of disabling stroke (>3 mRS) or reoperation to replace or remove a malfunctioning device**

Baseline Characteristics - 1

Characteristic	HeartMate 3 (n=190)	HeartMate II (n=176)
Age - years		
Mean	61 ± 12	59 ± 12
Median (range)	65 (19-81)	61 (24-84)
Male sex - no. (%)	150 (78.9)	143 (81.2)
Race or ethnic group - no. (%)		
White	127 (66.8)	131 (74.4)
Black or African American	52 (27.4)	32 (18.2)
Other*	11 (5.8)	13 (7.4)
Body surface area - m^2	2.1 ± 0.3	2.1 ± 0.3
Ischemic cause of heart failure - no. (%)	80 (42.1)	88 (50.0)
History of atrial fibrillation - no. (%)	81 (42.6)	83 (47.2)
History of stroke - no. (%)	16 (8.4)	20 (11.4)
Previous cardiac surgical procedure - no. (%)		
Coronary-artery bypass	44 (23.2)	41 (23.3)
History of valve replacement or repair	18 (9.5)	7 (4.0)
Concomitant medication or intervention - no (%)		
Intravenous inotropic agents	167 (87.9)	152 (86.4)
Diuretic	166 (87.4)	165 (93.8)
ACE inhibitor or Angiotensin II-receptor antagonist	58 (30.5)	66 (37.5)
Beta-blocker	111 (58.4)	98 (55.7)
CRT/CRT-D	75 (39.5)	62 (35.2)
ICD/CRT-D	122 (64.2)	123 (69.9)
IABP	25 (13.2)	26 (14.8)

There were significant differences between groups for history of valve replacement or repair (P=0.04) and diuretic use (P=0.05).
*Includes Asian, Native Hawaiian or Pacific Islanders, and other. CRT(-D) denotes cardiac resynchronization therapy with or without defibrillator; ICD, implantable cardioverter-defibrillator; IABP, intraaortic balloon pump.

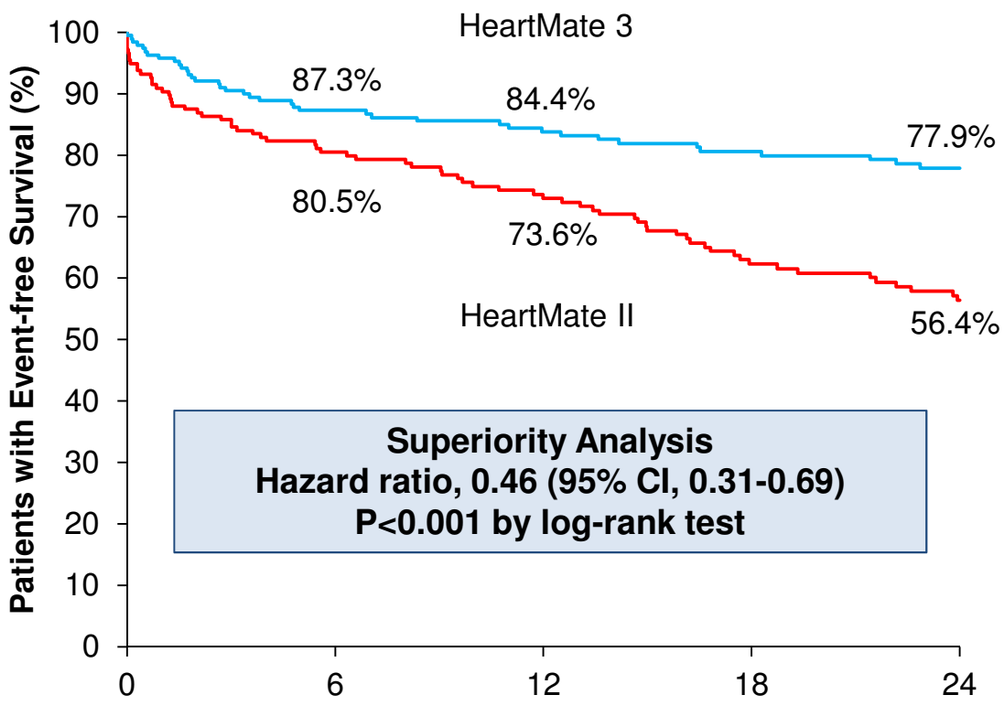
Baseline Characteristics - 2

Characteristic	HeartMate 3 (n=190)	HeartMate II (n=176)
Left ventricular ejection fraction - %	17.2 ± 4.9	17.4 ± 5.0
Arterial blood pressure - mmHg		
Systolic	110.2 ± 15.6	106.3 ± 12.9
Diastolic	67.0 ± 10.8	65.4 ± 10.4
Mean arterial pressure - mmHg	79.5 ± 10.1	78.4 ± 9.8
PCWP - mmHg	23.9 ± 8.6	22.2 ± 9.2
Cardiac index - liters/min/m^2 of body-surface area	2.0 ± 0.5	2.0 ± 0.7
PVR - Wood units	3.2 ± 1.7	3.0 ± 1.6
Right atrial pressure - mmHg	11.0 ± 6.5	10.5 ± 6.7
Serum sodium - mmol/liter	135.5 ± 3.8	135.2 ± 4.1
Serum creatinine - mg/dl	1.4 ± 0.4	1.4 ± 0.4
INTERMACS profile – no (%)		
1	1 (0.5)	4 (2.3)
2	61 (32.1)	51 (29.0)
3	101 (53.2)	91 (51.7)
4	24 (12.6)	28 (15.9)
5-7 or not provided	3 (1.6)*	2 (1.1)
Intended goal of pump support – no (%)		
Bridge to transplantation (BTT)	49 (25.8)	42 (23.9)
Bridge to candidacy for transplantation	30 (15.8)	28 (15.9)
Destination therapy (DT)	111 (58.4)	106 (60.2)

*One patient died before assessment was performed. There were only significant differences between groups for systolic blood pressure (P=0.01).
PCWP denotes pulmonary-capillary wedge pressure; PVR, pulmonary vascular resistance; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

Primary End Point Analysis (ITT)

Survival at 2 years free of disabling stroke (>3 mRS) or reoperation to replace or remove a malfunctioning device



No. at Risk					
HeartMate 3	190	161	141	122	111
HeartMate II	176	134	114	90	75

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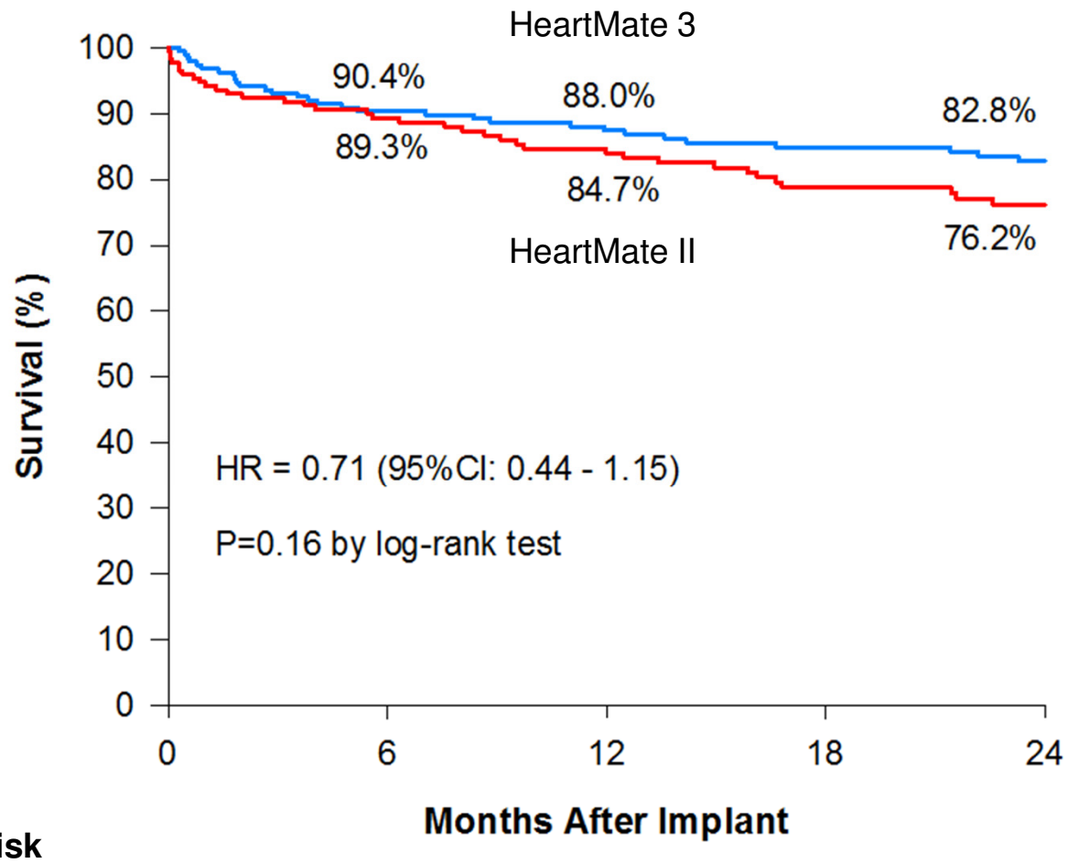
mRS denotes modified Rankin Score; CI, confidence interval

Primary Endpoint Component 1
Overall Survival



No. at Risk					
HeartMate 3	189	165	146	127	117
HeartMate II	172	141	121	98	86

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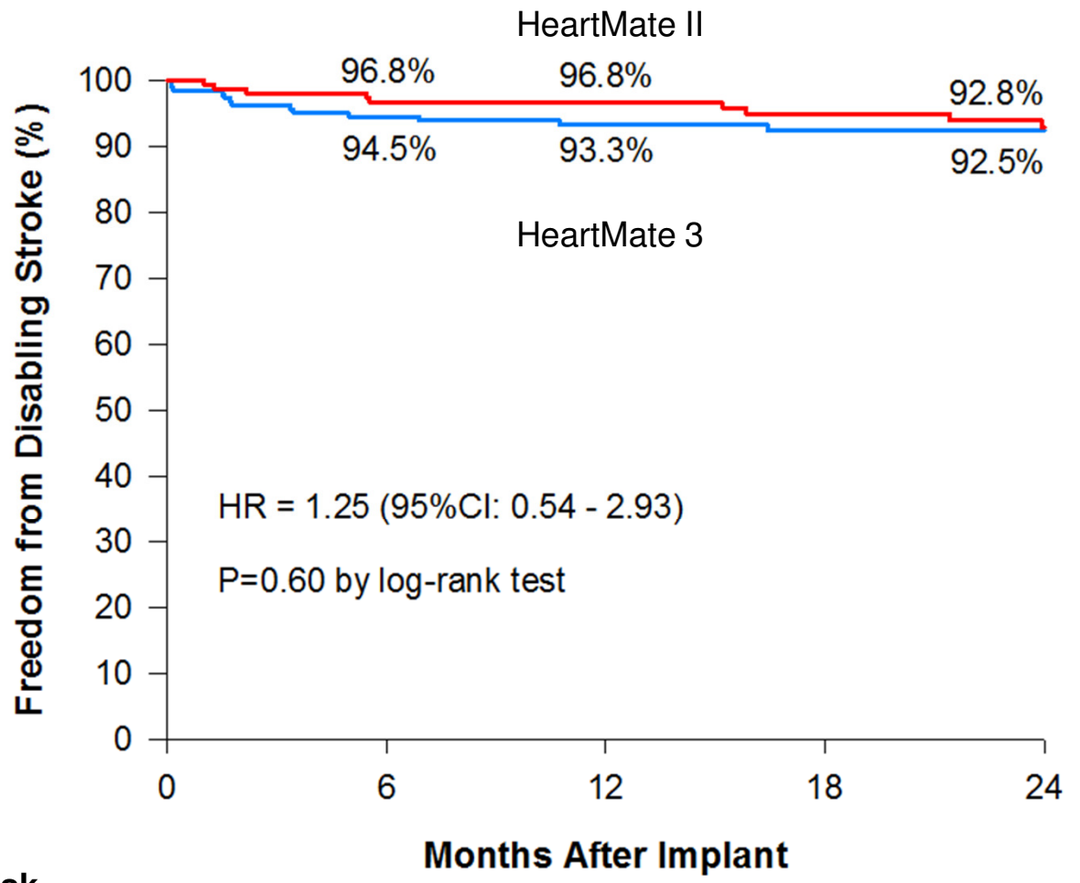
HR denotes hazard ratio; CI, confidence interval

Primary Endpoint Component 2
Freedom from Disabling Stroke



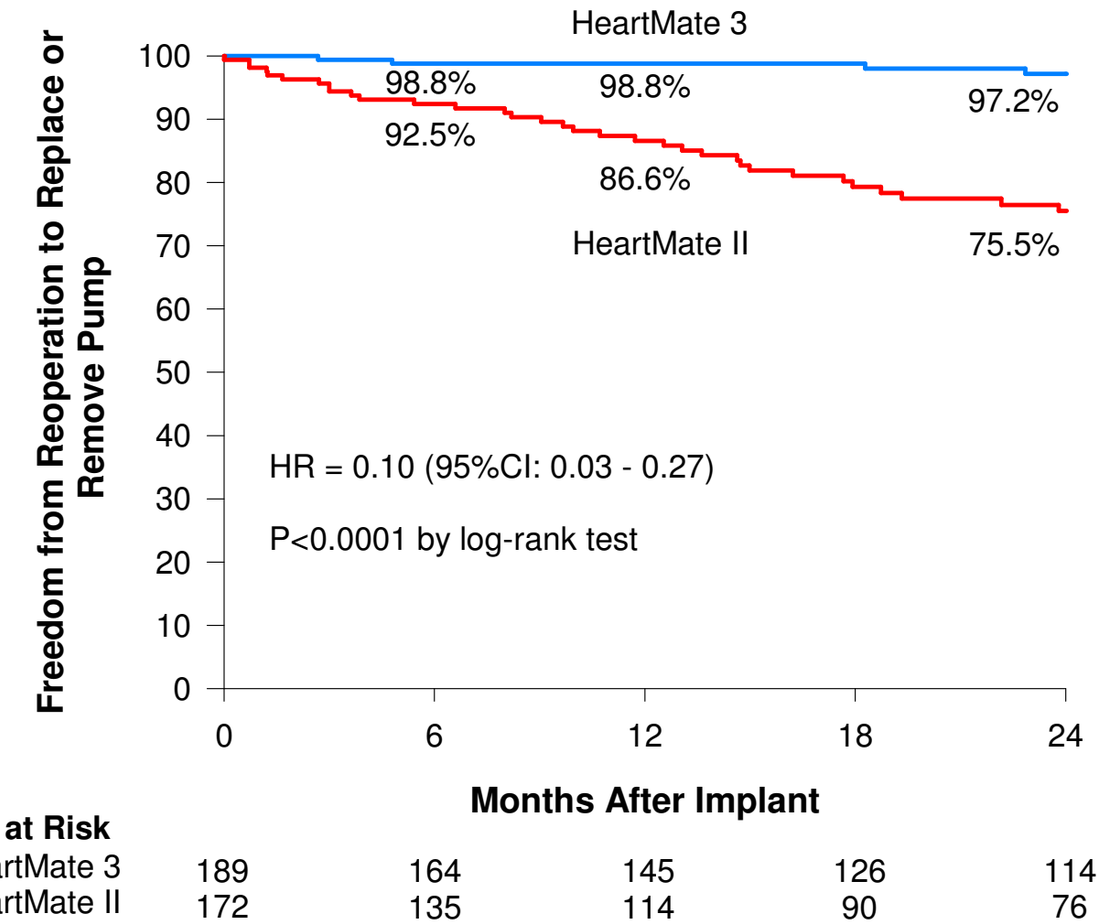
No. at Risk					
HeartMate 3	189	162	142	123	114
HeartMate II	172	139	121	97	84

MOMENTUM 3

HR denotes hazard ratio; CI, confidence interval

Primary Endpoint Component 3

Freedom from Reoperation to Replace or Remove Pump



No. at Risk

HeartMate 3	189	164	145	126	114
HeartMate II	172	135	114	90	76

- There was a **ten-fold** difference in the reoperation rate between HeartMate II and HeartMate 3
- HeartMate 3 reoperations were due to **infection** (1), **electrical fault** (1), and **outflow-graft twist** (1)
- **2/3rd** of HeartMate II reoperations were due to “pump thrombosis or severe hemolysis”

MOMENTUM 3

HR denotes hazard ratio, CI, confidence interval

Key Adverse Events

Pump Thrombosis, Neurological Events, Bleeding

	HeartMate 3 (n=189)		HeartMate II (n=172)			
	n (%)	no. of Events	n (%)	no. of Events	HR (95% CI)	P Value*
Suspected or confirmed pump thrombosis	2 (1.1)	2	27 (15.7)	33	0.06 (0.01-0.26)	<0.001
Resulting in reoperation	0 (0)	0	21 (12.2)	25	NA	<0.001
Any stroke	19 (10.1)	22	33 (19.2)	43	0.47 (0.27-0.84)	0.02
Ischemic stroke	12 (6.3)	14	23 (13.4)	26	0.44 (0.22-0.88)	0.03
Hemorrhagic stroke	8 (4.2)	8	16 (9.3)	17	0.42 (0.18-0.98)	0.06
Other neurologic event+	22 (11.6)	25	15 (8.7)	16	1.27 (0.66-2.45)	0.39
Bleeding	81 (42.9)	187	90 (52.3)	206	0.71 (0.53-0.96)	0.07
Bleeding that led to surgery	23 (12.2)	29	30 (17.4)	34	0.66 (0.38-1.13)	0.18
Gastrointestinal bleeding	51 (27.0)	107	47 (27.3)	100	0.92 (0.62-1.37)	1.00

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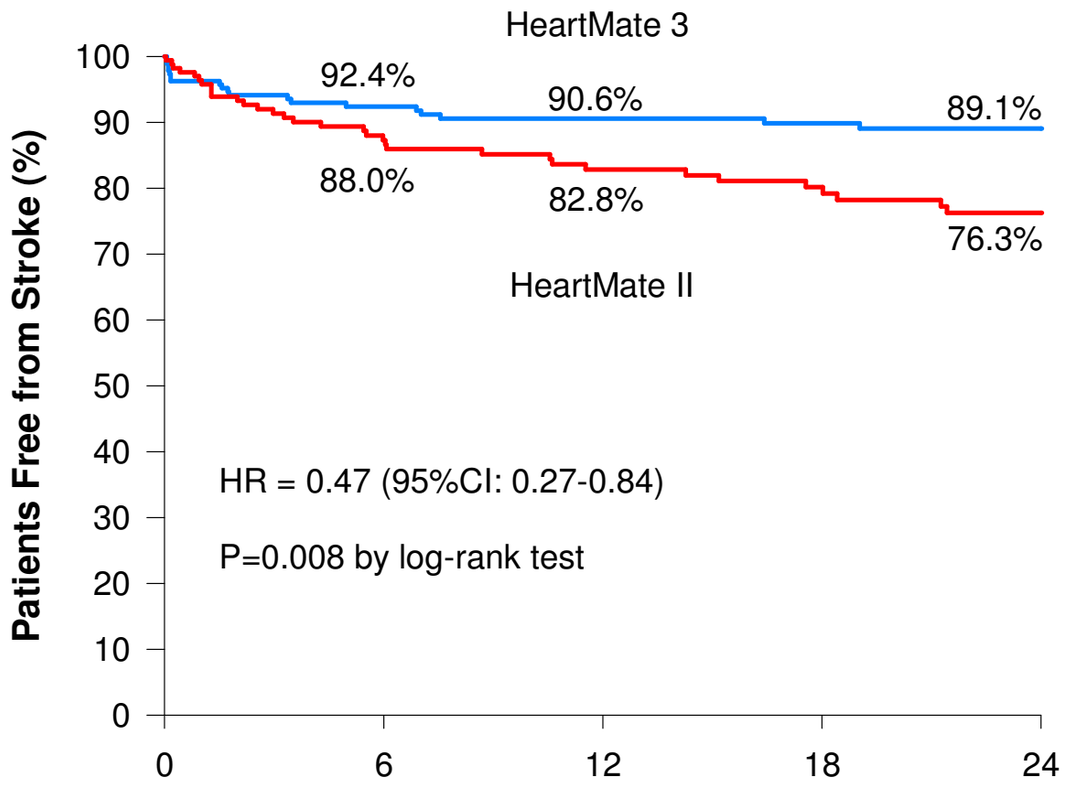
HR denotes hazard ratio; CI, confidence interval

*P values were calculated with the use of Fisher's exact test. +Includes transient ischemic attacks and neurologic events other than stroke

Key Adverse Events
Stroke



No. at Risk					
HeartMate 3	189	159	138	120	111
HeartMate II	172	127	104	85	73

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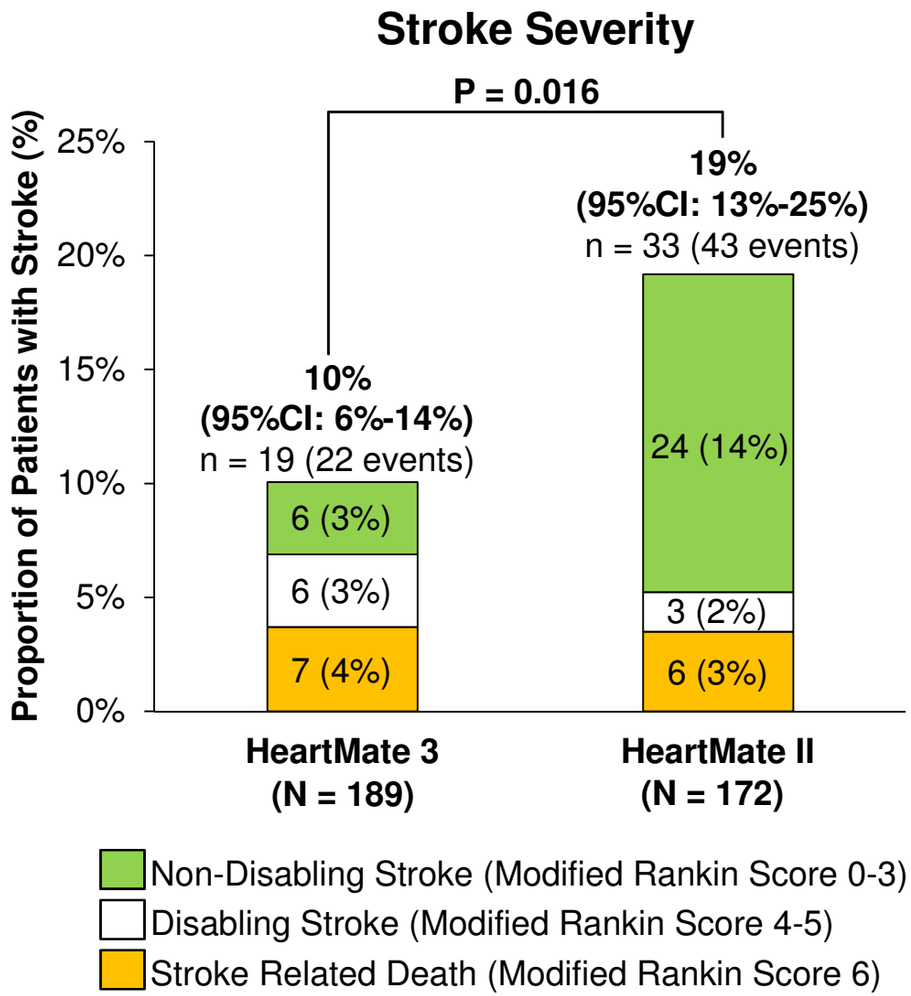
Key Adverse Events
Stroke



Two HeartMate 3 subjects and 9 HeartMate II subjects had >1 stroke. The score for the most severe stoke is shown. 1.6% of HeartMate 3 subjects (n = 3) and 5.2% of HeartMate II subjects (n = 9) had a modified Rankin score of 0 at 60 days post-stroke. CI denotes confidence interval.

Other Adverse Events

	HeartMate 3 (n=189)		HeartMate II (n=172)			
	n (%)	no. of Events	n (%)	no. of Events	HR (95% CI)	P Value
Sepsis	26 (13.8)	37	24 (14.0)	28	0.95 (0.55-1.66)	1.00
LVAS drive-line infection	45 (23.8)	68	34 (19.8)	59	1.15 (0.73-1.79)	0.37
Local non-LVAS infection	70 (37.0)	108	60 (34.9)	114	1.00 (0.71-1.42)	0.74
Right heart failure	60 (31.7)	73	48 (27.9)	53	1.12 (0.77-1.64)	0.49
Managed with RVAS	6 (3.2)	6	8 (4.7)	8	0.67 (0.23-1.94)	0.59
Cardiac arrhythmia	71 (37.6)	108	70 (40.7)	105	0.88 (0.63-1.23)	0.59
Ventricular	45 (23.8)	67	39 (22.7)	64	1.04 (0.67-1.59)	0.80
Supraventricular	33 (17.5)	40	36 (20.9)	37	0.79 (0.49-1.26)	0.42
Respiratory failure	45 (23.8)	61	39 (22.7)	46	1.04 (0.68-1.59)	0.80
Renal Dysfunction	25 (13.2)	29	18 (10.5)	18	1.23 (0.67-2.25)	0.52
Hepatic dysfunction	8 (4.2)	8	7 (4.1)	7	0.98 (0.36-2.71)	1.00

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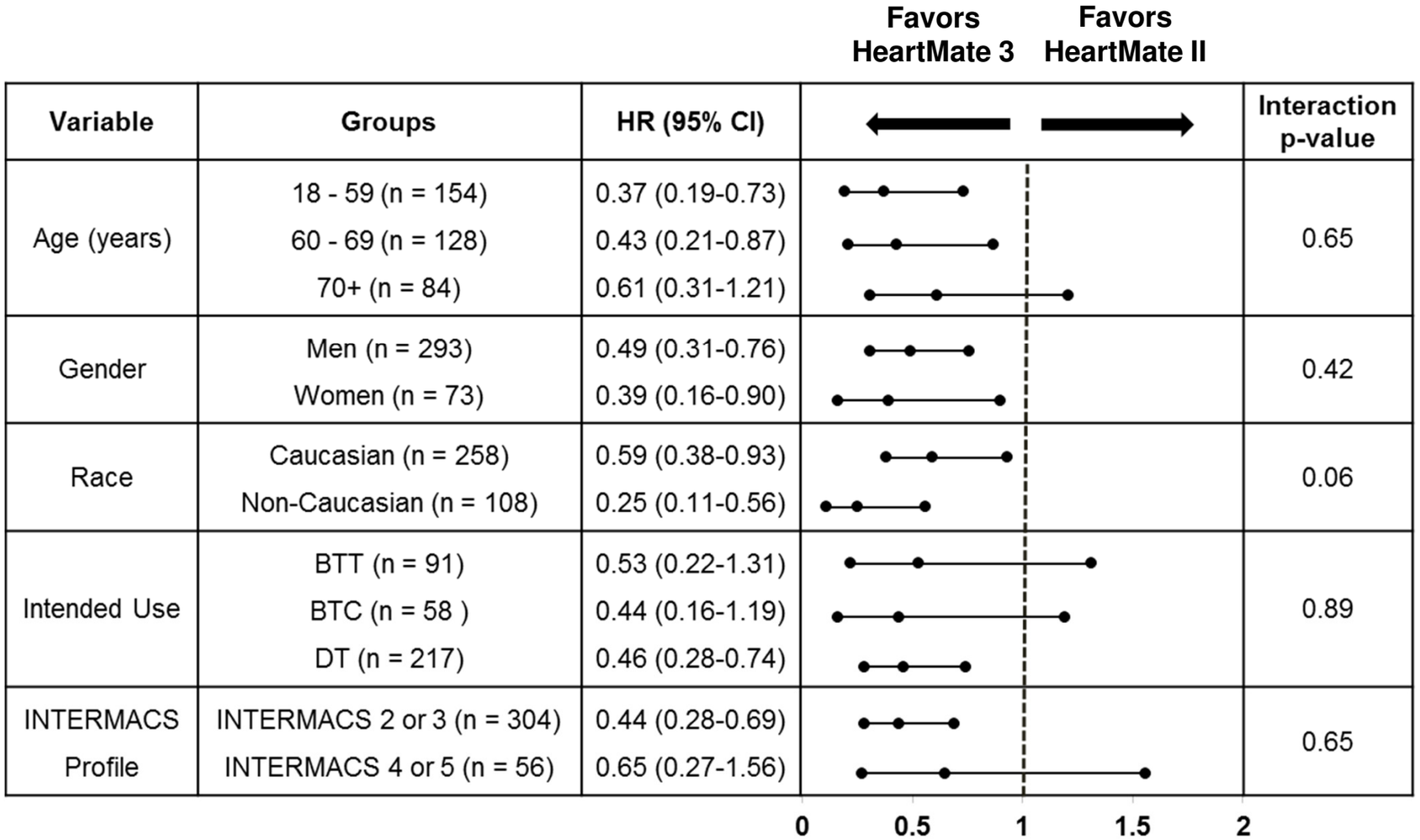
LVAS denotes Left Ventricular Assist System, RVAD, Right Ventricular Assist Device, HR, Hazard Ratio, and CI, confidence interval.

Subgroup Analyses of the Primary Endpoint (ITT)



Variable	Groups	HR (95% CI)	Interaction p-value
Age (years)	18 - 59 (n = 154)	0.37 (0.19-0.73)	0.65
	60 - 69 (n = 128)	0.43 (0.21-0.87)	
	70+ (n = 84)	0.61 (0.31-1.21)	
Gender	Men (n = 293)	0.49 (0.31-0.76)	0.42
	Women (n = 73)	0.39 (0.16-0.90)	
Race	Caucasian (n = 258)	0.59 (0.38-0.93)	0.06
	Non-Caucasian (n = 108)	0.25 (0.11-0.56)	
Intended Use	BTT (n = 91)	0.53 (0.22-1.31)	0.89
	BTC (n = 58)	0.44 (0.16-1.19)	
	DT (n = 217)	0.46 (0.28-0.74)	
INTERMACS Profile	INTERMACS 2 or 3 (n = 304)	0.44 (0.28-0.69)	0.65
	INTERMACS 4 or 5 (n = 56)	0.65 (0.27-1.56)	

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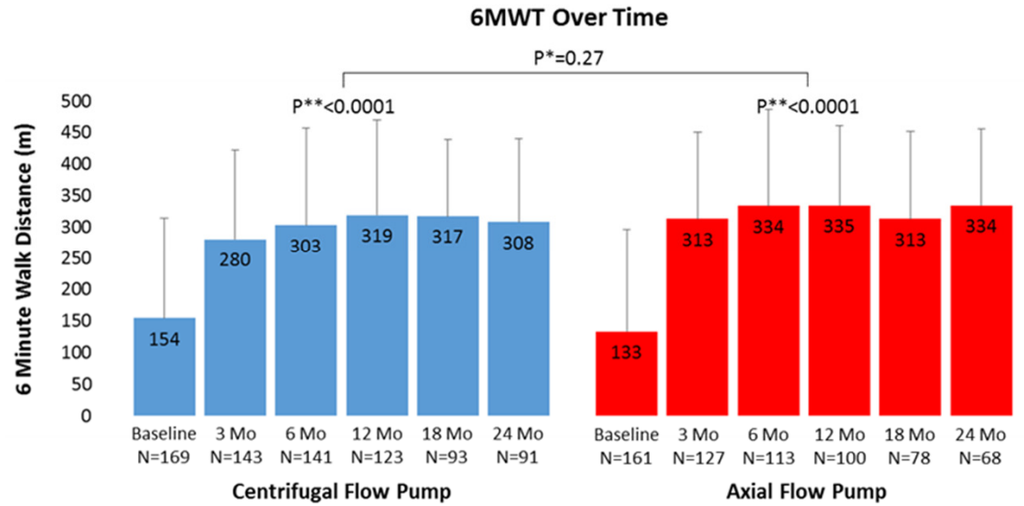
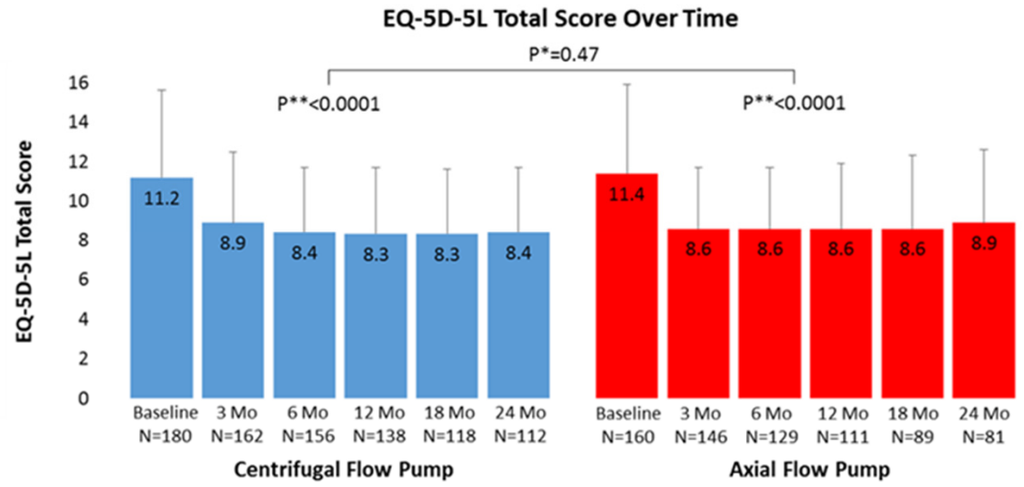
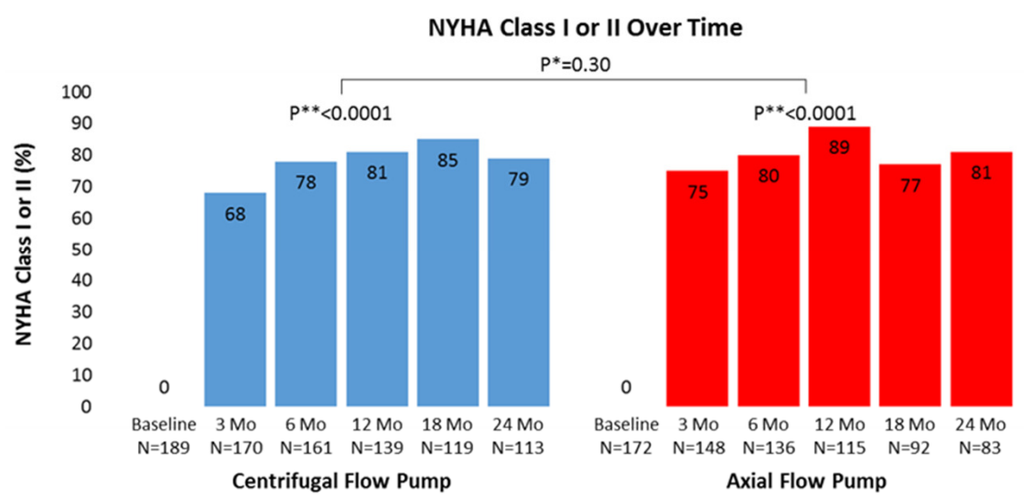
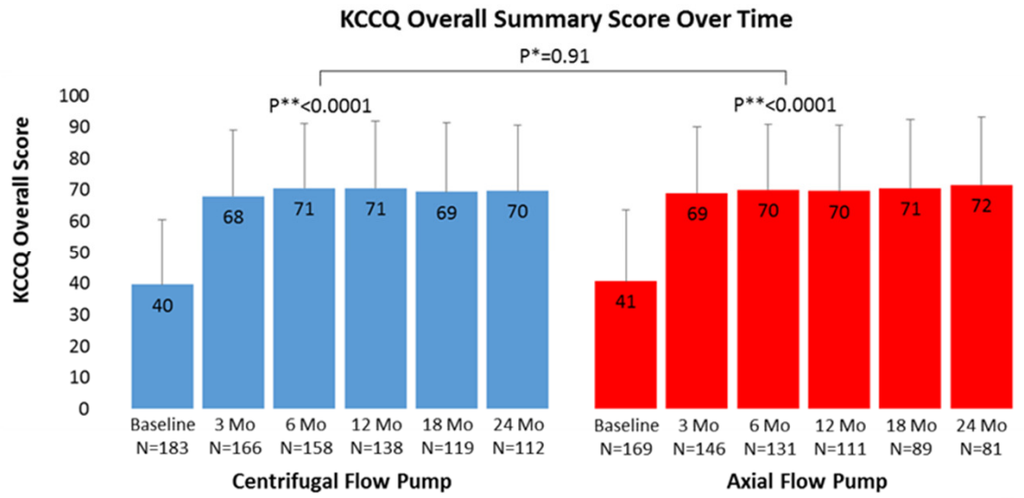
BTT denotes bridge to transplant; BTC, bridge to candidacy; DT, destination therapy

Functional Status and Quality of Life









*P-value between treatment arms over time
**P-value for treatment over time

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Conclusions

- The HeartMate 3 LVAS is **clinically superior** when compared to the HeartMate II axial-flow pump, at 2-years

- These benefits were primarily driven by a **lower reoperation rate** in the HeartMate 3 arm
  - largely due to excess device malfunctions resulting from **pump thrombosis** in the HeartMate II LVAS

- Importantly, we observed a markedly **lower rate of stroke** with the HeartMate 3 LVAS

Summary

The two-year MOMENTUM 3 trial pre-specified primary analysis demonstrates durability of the HeartMate 3 LVAS to optimally support patients who wait for extended periods for heart transplantation or are ineligible for heart transplantation (destination therapy)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two-Year Outcomes of a Magnetically Levitated Cardiac Pump in Heart Failure

M.R. Mehra, D.J. Goldstein, N. Uriel, J.C. Cleveland, Jr., M. Yuzefpolskaya, C. Salerno, M.N. Walsh, C.A. Milano, C.B. Patel, G.A. Ewald, A. Itoh, D. Dean, A. Krishnamoorthy, W.G. Cotts, A.J. Tatooles, U.P. Jorde, B.A. Bruckner, J.D. Estep, V. Jeevanandam, G. Sayer, D. Horstmanshof, J.W. Long, S. Gulati, E.R. Skipper, J.B. O'Connell, G. Heatley, P. Sood, and Y. Naka, for the MOMENTUM 3 Investigators*

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We THANK all the patients, our investigators, clinical nurse coordinators, and allied health personnel for their dedication to the conduct of the MOMENTUM 3 trial

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