A Fully Magnetically Levitated Left Ventricular Assist Device

Final Report of the MOMENTUM 3 Trial

Mandeep R. Mehra, MD, Nir Uriel, MD, Joseph C. Cleveland, Jr., MD, Daniel J. Goldstein, MD,

National Principal Investigators, on behalf of the MOMENTUM 3 Investigators

MOMENTUM 3

Disclosures

- Dr. Mandeep R. Mehra:

  Consultant for Abbott, Portola, Bayer, and Xogenex. Trial steering committee member for Medtronic and Janssen. Scientific advisory board member for NupulseCV and FineHeart. DSMB member for Mesoblast. Travel support from Abbott.

- Dr. Nir Uriel:

  Research grants from Abbott and Medtronic. Consultant for Abbott and Medtronic.

- Dr. Joseph C. Cleveland, Jr.:

  Institutional research grants from Abbott.

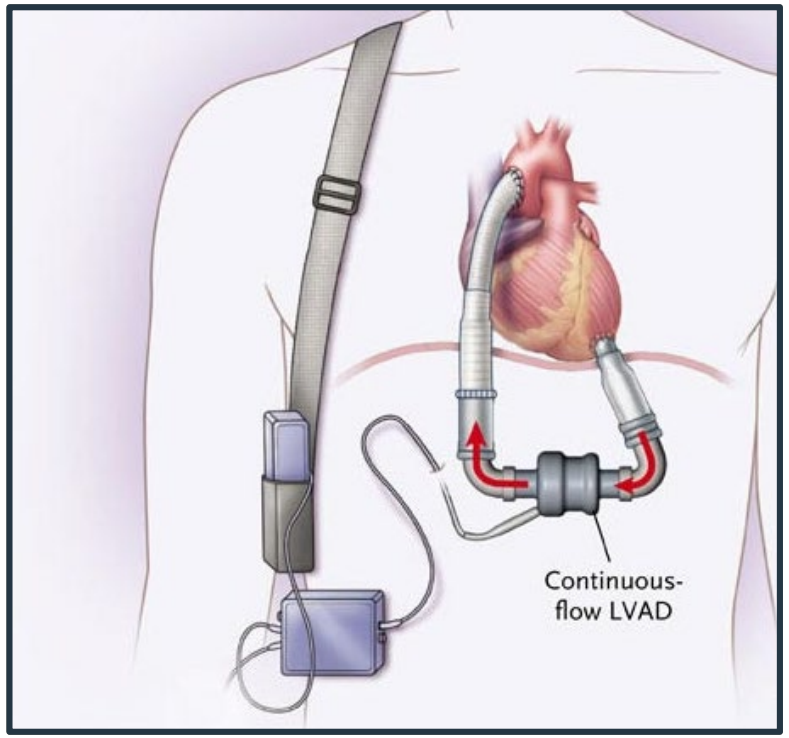
- Dr. Daniel J. Goldstein:

  Proctor and educator for Abbott. Travel support from Abbott. DSMB member for TERUMO Inc.

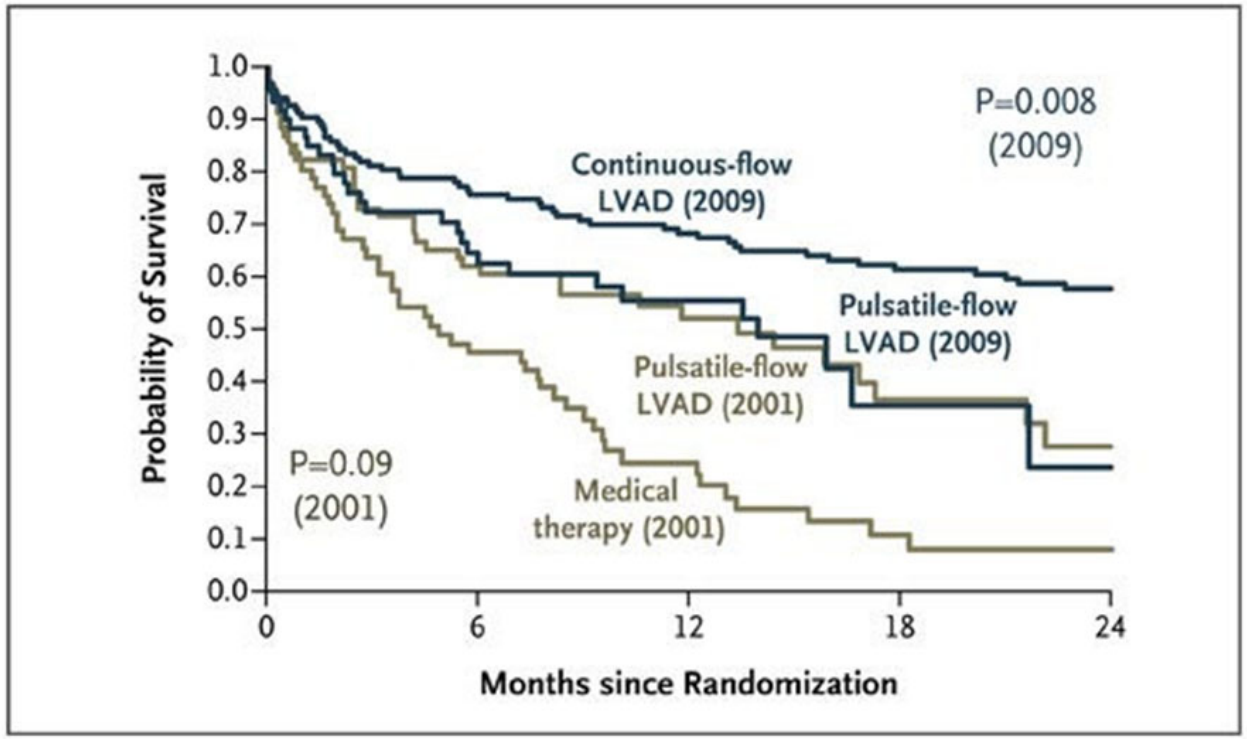
- MOMENTUM 3 is sponsored by Abbott (ClinicalTrials.gov NCT02224755)

Background

- **Left Ventricular Assist Systems (LVAS) improve survival and quality of life in patients with advanced heart failure refractory to medical therapy[1,2]**



HeartMate II: Continuous-flow LVAD



Fang JC. *N Engl J Med* 2009;361(23):2282-5

MOMENTUM 3

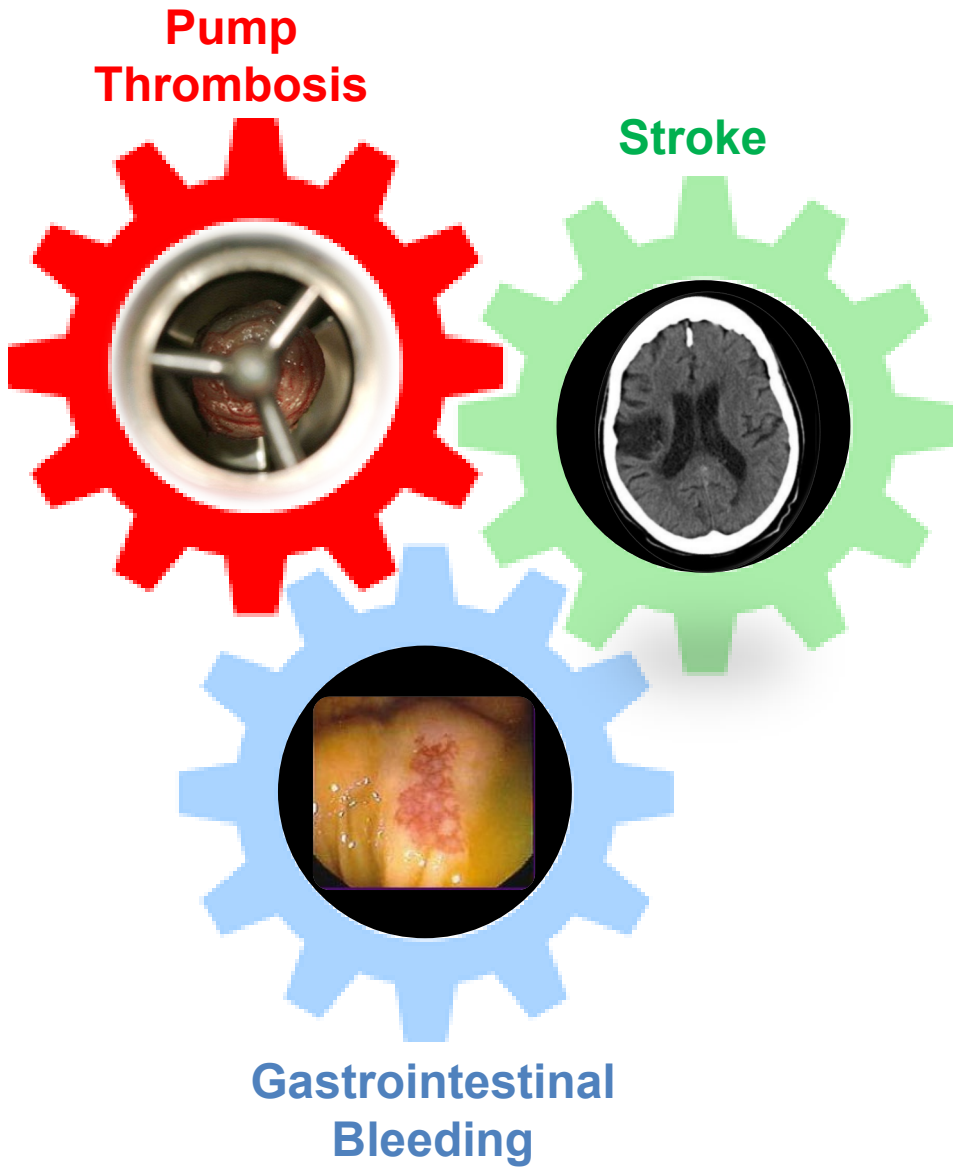
[1]Rose EA et al. Long-Term Use of a Left Ventricular Assist Device for End-Stage Heart Failure. *N Engl J Med* 2001;345(20):1435-43

[2]Slaughter MS et al. Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device. *N Engl J Med* 2009;361(23):2241-51

Background

- Despite improving survival and quality of life, patients with continuous-flow LVADs are burdened with *hemocompatibility-related complications*[1]

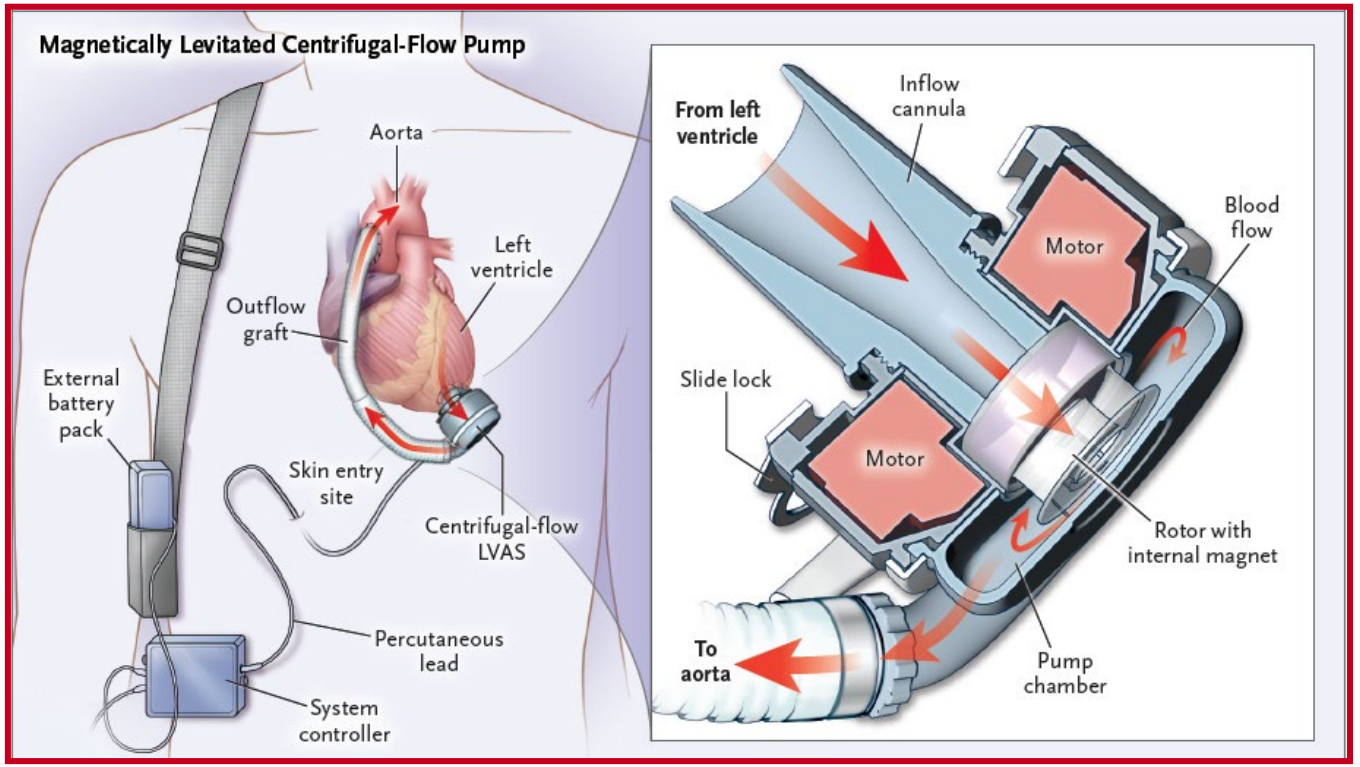
- Consequences of adverse interactions between the *pump and circulating blood elements*
  - Pump thrombosis
  - Stroke
  - Gastrointestinal bleeding



MOMENTUM 3

[1]Mehra MR. The burden of haemocompatibility with left ventricular assist systems: a complex weave. Eur Heart J 2019;40(8):673-7

HeartMate 3 LVAS

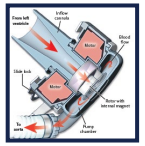


- **Wide** blood-flow passages to reduce shear stress
- **Frictionless** with absence of mechanical bearings
- **Intrinsic Pulse** designed to reduce stasis and avert thrombosis

MOMENTUM 3

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

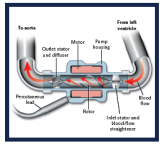
Adaptive Trial Design



HeartMate 3

Advanced Heart Failure Irrespective of Intended Goal of Therapy

(Bridge to Transplant or Destination Therapy)



HeartMate II

Randomization 1:1

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

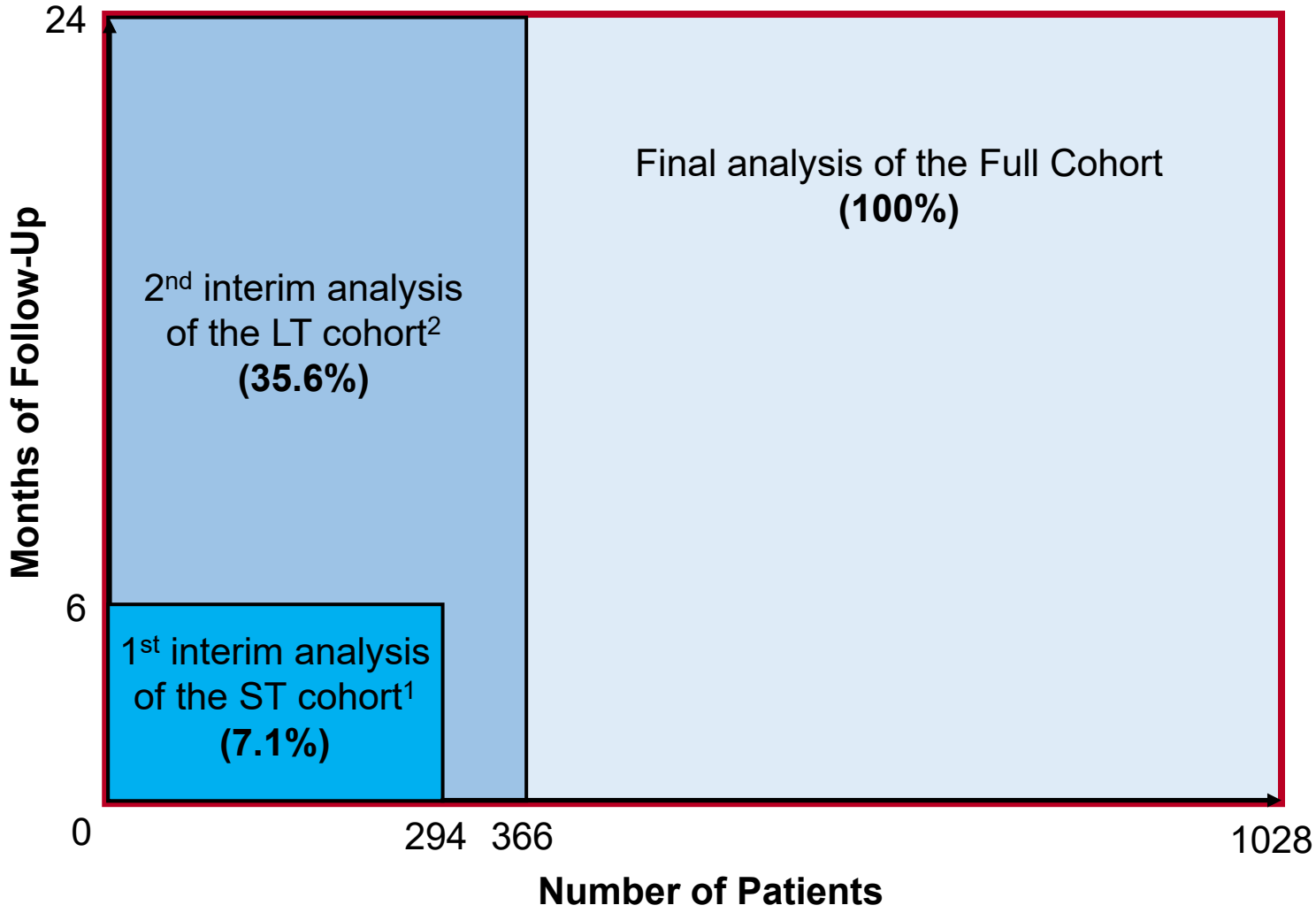
Additional 72 patients enrolled

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

Additional 662 patients enrolled

Full Cohort
N=1028
2-year follow-up

Net Trial Experience



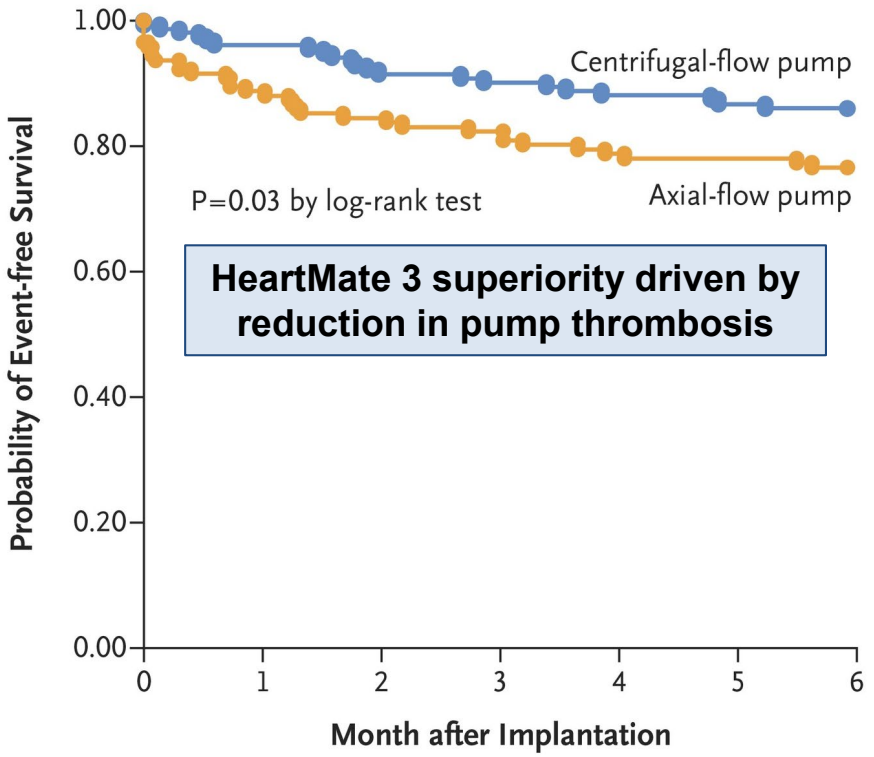
MOMENTUM 3

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

[2]Mehra MR et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *N Engl J Med* 2018;378(15):1386-95

Two Interim Analyses

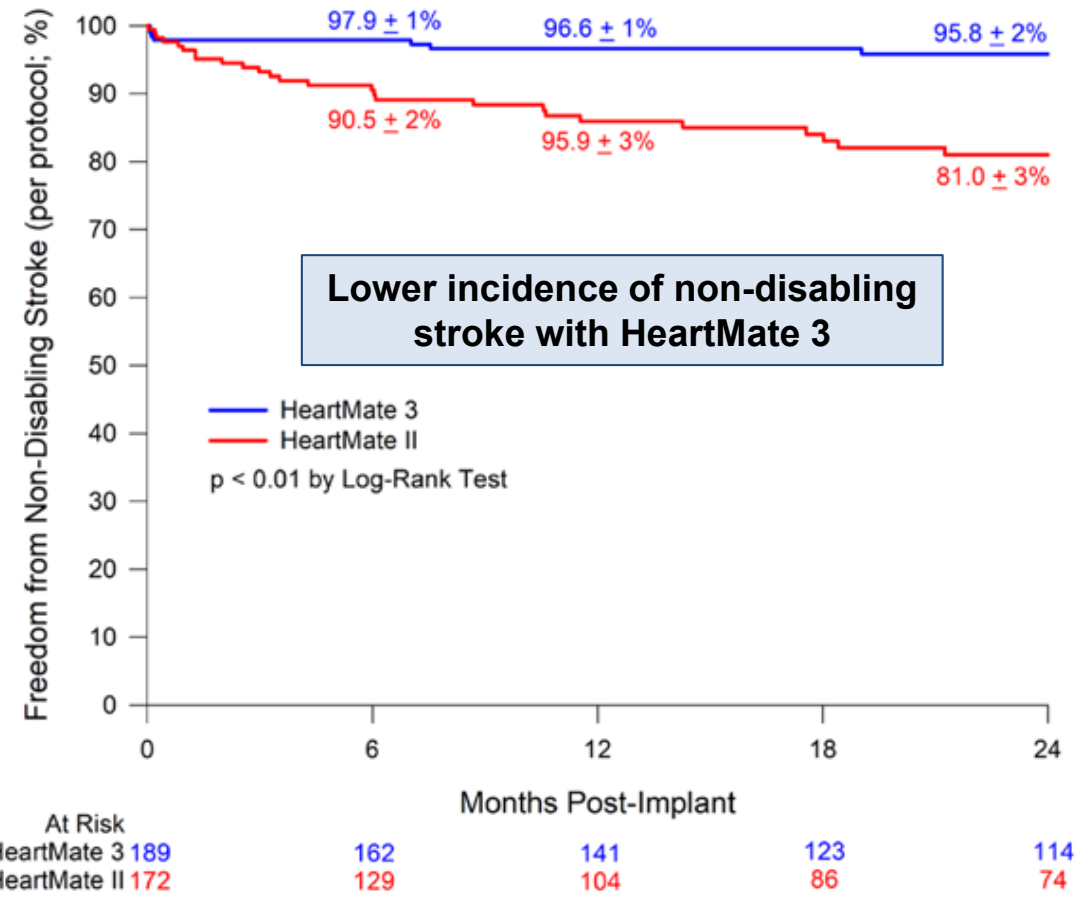
ST Cohort: 294 Patients at 6 Months[1]



HeartMate 3 superiority driven by reduction in pump thrombosis

No. at Risk							
Centrifugal-flow pump	152	146	138	135	130	128	127
Axial-flow pump	142	125	119	116	110	106	103

LT Cohort: 366 Patients at 2 Years[2,3]



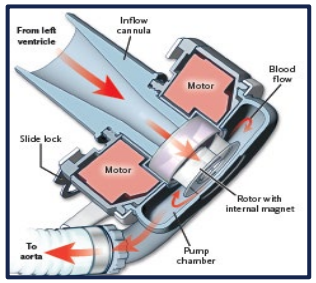
Lower incidence of non-disabling stroke with HeartMate 3

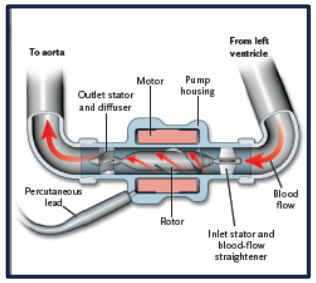
At Risk					
HeartMate 3	189	162	141	123	114
HeartMate II	172	129	104	86	74

[1]Mehra MR et al. A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure. *N Engl J Med* 2017;376(5):440-50.
[2]Mehra MR et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *N Engl J Med* 2018;378(15):1386-95
[3]Colombo PC et al. Comprehensive Analysis of Stroke in the Long-Term Cohort of the MOMENTUM 3 Study. *Circ* 2019;139 (2):155-68

MOMENTUM 3

Full Cohort





Full Cohort
N=1028
24-month follow-up

HeartMate 3
N=516

HeartMate II
N=512

Intent-to-Treat (ITT) Population
N=1028

Withdrawn before implant
N = 1
Death: 1

Withdrawn before implant
N = 7
Death: 2
No LVAD implant: 2
Withdrawal of consent: 1
Transplant: 1
Implanted with non-study LVAD: 1

As-Treated Population
N=1020

Implanted with HeartMate 3
N=515

Implanted with HeartMate II
N=505

Withdrawn after implant
N = 6
Implanted with non-study device: 2
Withdrawal of consent: 1
Non-compliance: 1
Other reason: 2

Withdrawn after implant
N = 15
Implanted with non-study device: 5
Withdrawal of consent: 1
Implanted with HM3: 6
Other reason: 3

Completed study follow-up
N=509

Completed study follow-up
N=490

MOMENTUM 3

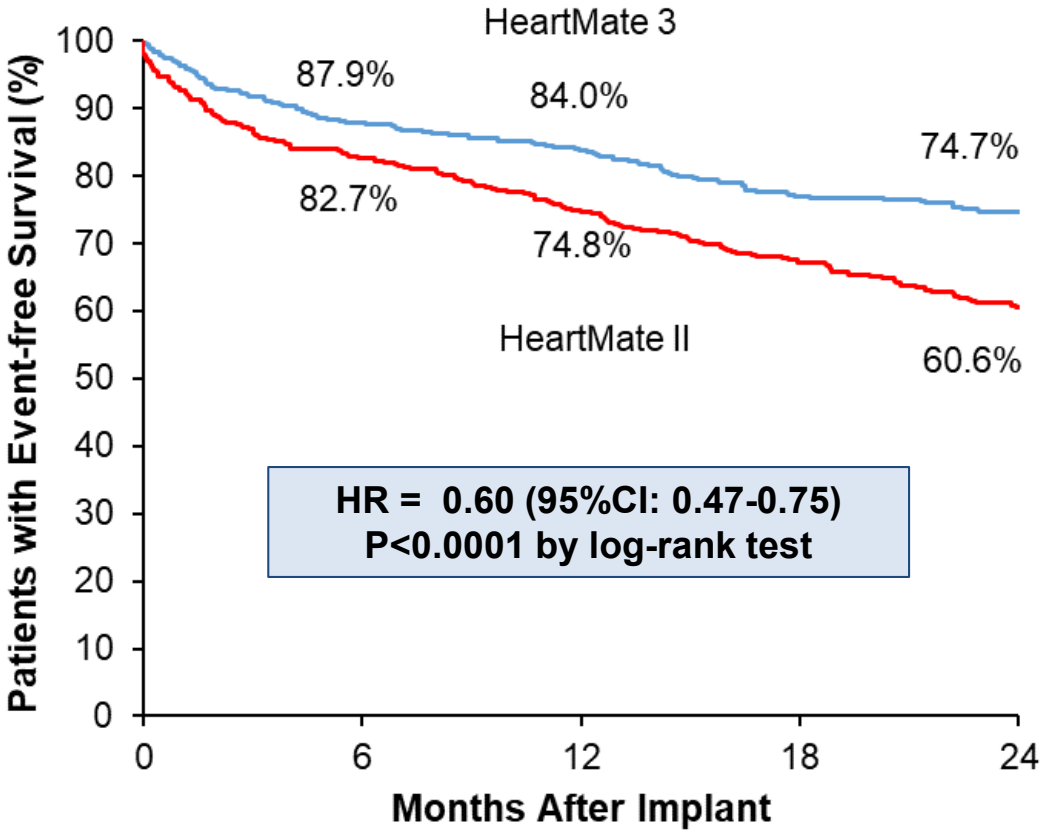
Baseline Characteristics

Characteristic	HeartMate 3 (n=516)	HeartMate II (n=512)
Mean age - years	59 ± 12	60 ± 12
Male - no. (%)	411 (79.7)	419 (81.8)
Race - no. (%)		
White	342 (66.3)	367 (71.7)
Black or African American	145 (28.1)	120 (23.4)
Asian	8 (1.6)	3 (0.6)
Native Hawaiian or Pacific islander	0 (0)	4 (0.8)
Other	21 (4.1)	18 (3.5)
Ischemic cause of heart failure - no. (%)	216 (41.9)	240 (46.9)
Intravenous inotropic agents - no. (%)	445 (86.2)	423 (82.6)
Intra aortic balloon pump - no. (%)	64 (12.4)	79 (15.4)
Serum creatinine - mg/dl	1.4 ± 0.4	1.4 ± 0.4
Serum sodium – mmol/liter	135.4 ± 4.1	135.5 ± 4.2
Mean arterial pressure - mmHg	79.2 ± 10.4	79.2 ± 10.1
INTERMACS profile - no. (%)		
1	11 (2.1)	18 (3.5)
2	156 (30.2)	146 (28.5)
3	272 (52.7)	251 (49.0)
4	67 (13.0)	82 (16.0)
5-7 or not provided*	10 (1.9)	15 (2.9)
Intended goal of pump support - no. (%)		
Bridge to transplantation (BTT)	113 (21.9)	121 (23.6)
Bridge to candidacy for transplantation	86 (16.7)	81 (15.8)
Destination therapy (DT)	317 (61.4)	310 (60.5)

There were significant differences between groups for race (P=0.04). *Assessments were not performed in 2 centrifugal-flow pump patients and 5 axial-flow pump patients.

Primary End Point (ITT)

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



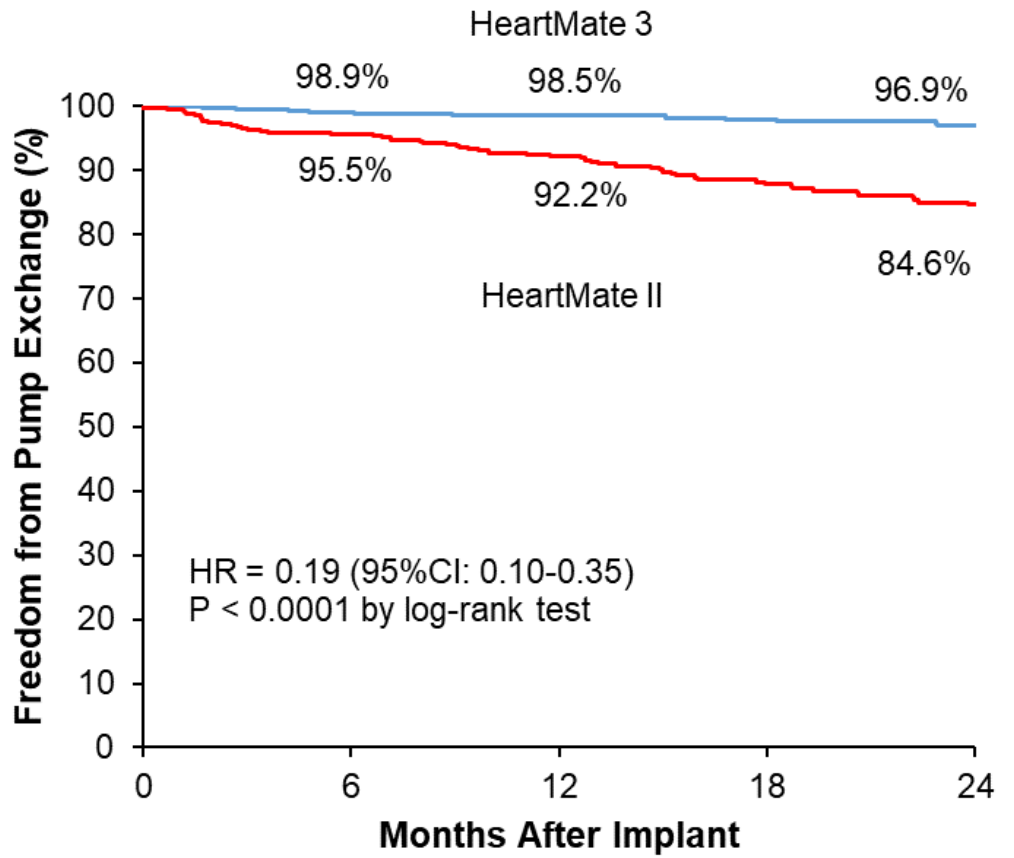
No. at Risk:					
HeartMate 3	516	438	373	313	280
HeartMate II	512	401	321	264	223

MOMENTUM 3

mRS denotes modified Rankin Score; HR, hazard ratio; CI, confidence interval

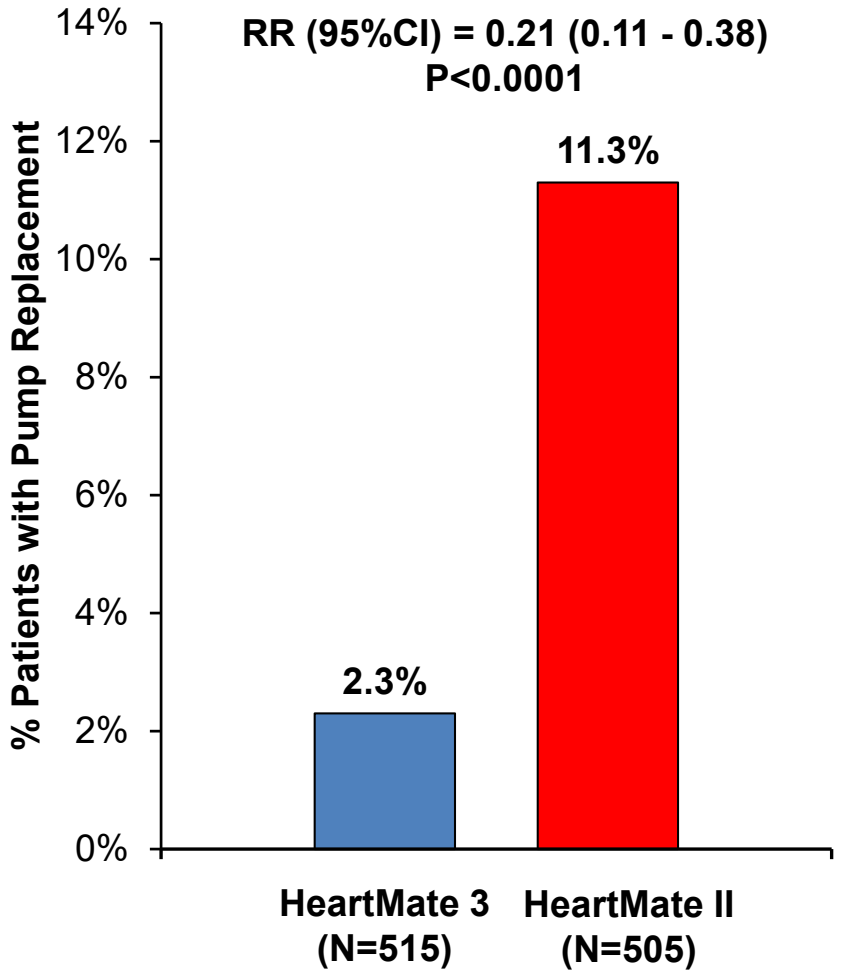
Principal Secondary End Point

Pump replacement at 2 years



No. at Risk:

HeartMate 3	515	444	379	317	283
HeartMate II	505	403	322	264	226

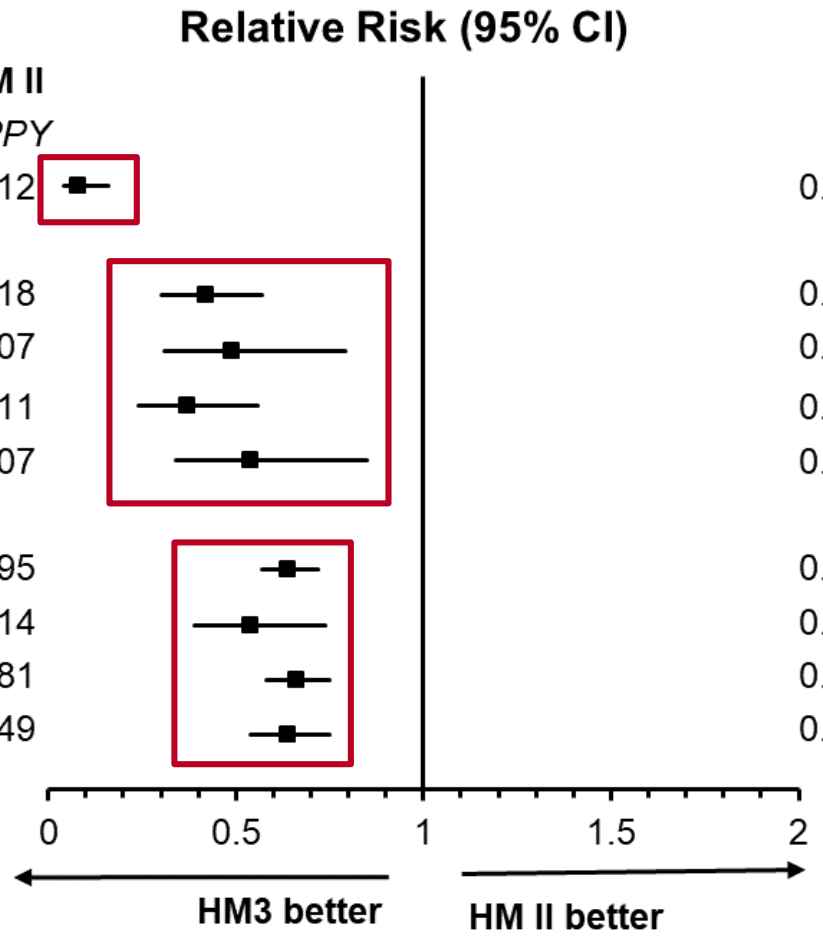


MOMENTUM 3

RR denotes relative risk; CI, confidence interval; HR, hazard ratio

Principal Hemocompatibility-Related Adverse Events

Adverse Event	HM3 n (%)	HM II n (%)	HM3 EPPY	HM II EPPY	Relative Risk (95% CI)	P-Value*
Suspected pump thrombosis	7 (1.4)	70 (13.9)	0.01	0.12	0.08 (0.04 - 0.16)	<0.0001
Any stroke	51 (9.9)	98 (19.4)	0.08	0.18	0.42 (0.30 - 0.57)	<0.0001
Hemorrhagic stroke	25 (4.9)	43 (8.5)	0.03	0.07	0.49 (0.31 - 0.79)	0.004
Ischemic stroke	29 (5.6)	65 (12.9)	0.04	0.11	0.37 (0.24 - 0.56)	<0.0001
Disabling stroke	26 (5.0)	38 (7.5)	0.04	0.07	0.54 (0.34 - 0.85)	0.008
Any bleeding	225 (43.7)	278 (55.0)	0.61	0.95	0.64 (0.57 - 0.72)	<0.0001
Requiring surgery	50 (9.7)	89 (17.6)	0.08	0.14	0.54 (0.39 - 0.74)	<0.001
Not requiring surgery	197 (38.3)	251 (49.7)	0.53	0.81	0.66 (0.58 - 0.75)	<0.0001
Gastrointestinal bleeding	126 (24.5)	156 (30.9)	0.31	0.49	0.64 (0.54 - 0.75)	<0.0001

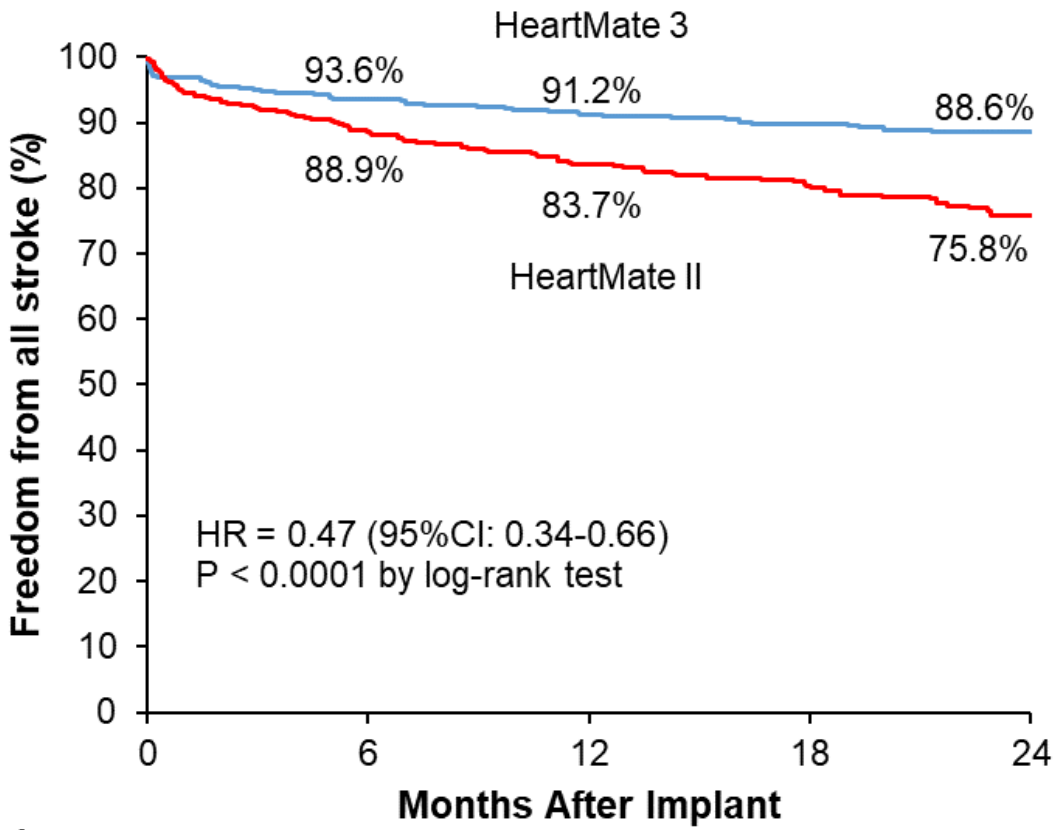


MOMENTUM 3

HM3 denotes HeartMate 3; HMII HeartMate II; EPPY events per patient year; CI, confidence interval. *P values were calculated with Poisson Regression.

Stroke

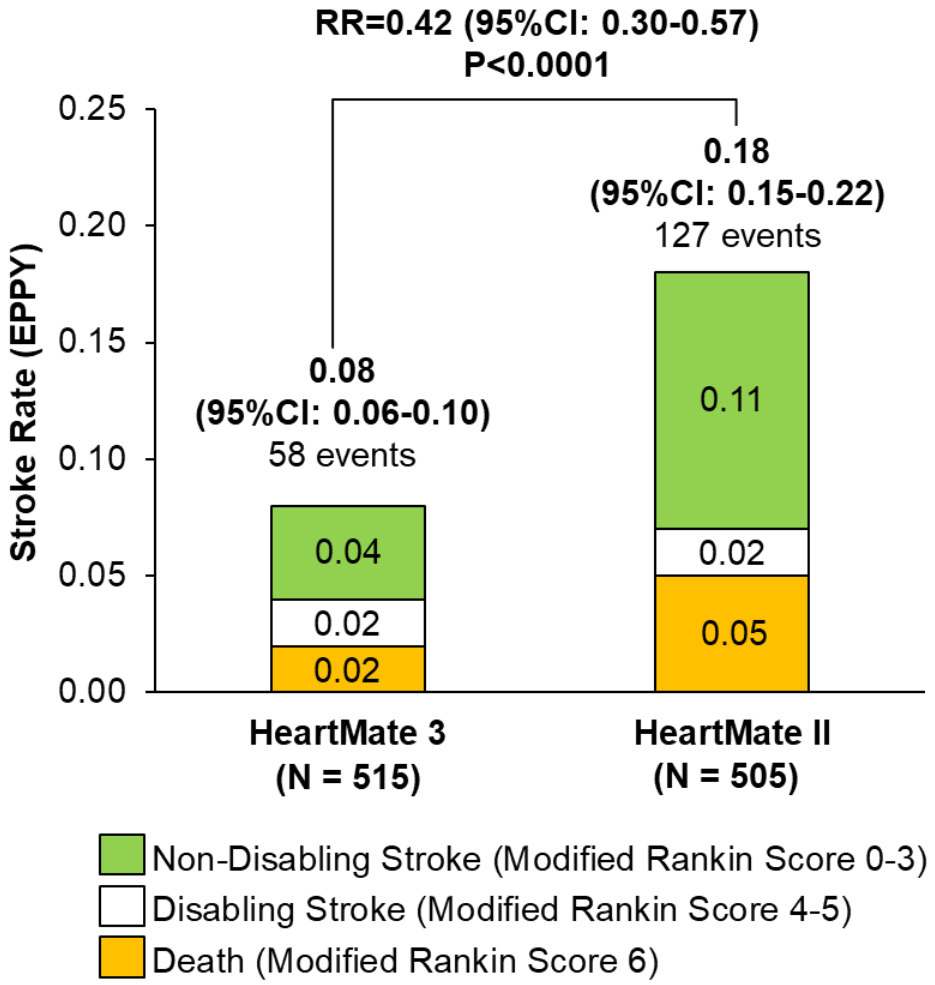
Freedom from All Stroke



No. at Risk:

HeartMate 3	515	429	361	304	270
HeartMate II	505	384	299	252	210

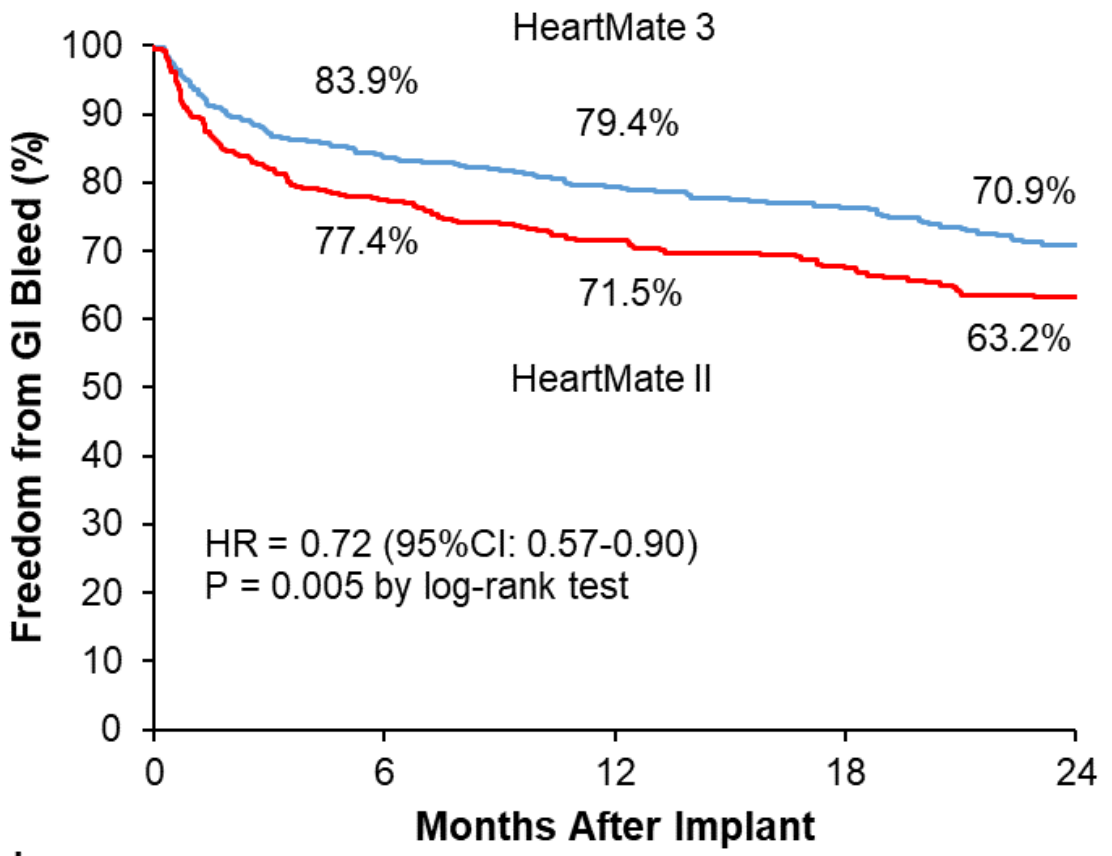
Stroke Severity



HR denotes hazard ratio; CI, confidence interval; RR, relative risk; EPPY, events per patient year

Gastrointestinal Bleeding

Freedom from Gastrointestinal Bleeding



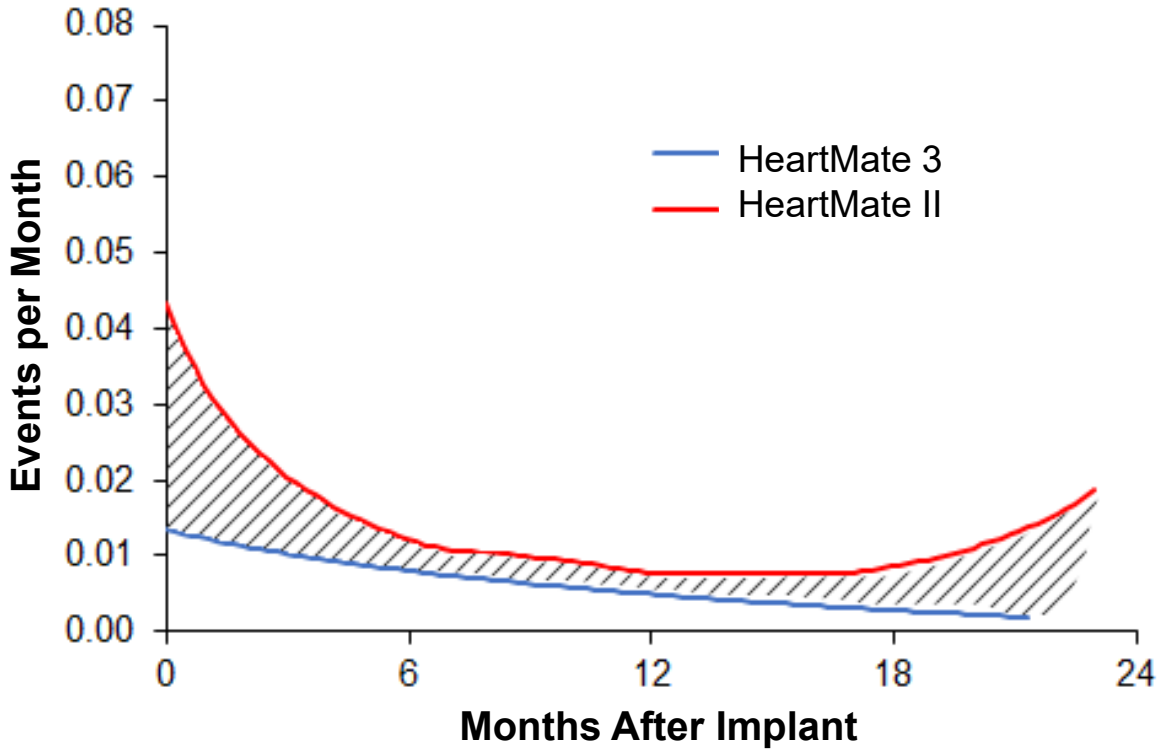
No. at Risk:					
HeartMate 3	515	381	308	251	204
HeartMate II	505	325	248	202	167

MOMENTUM 3

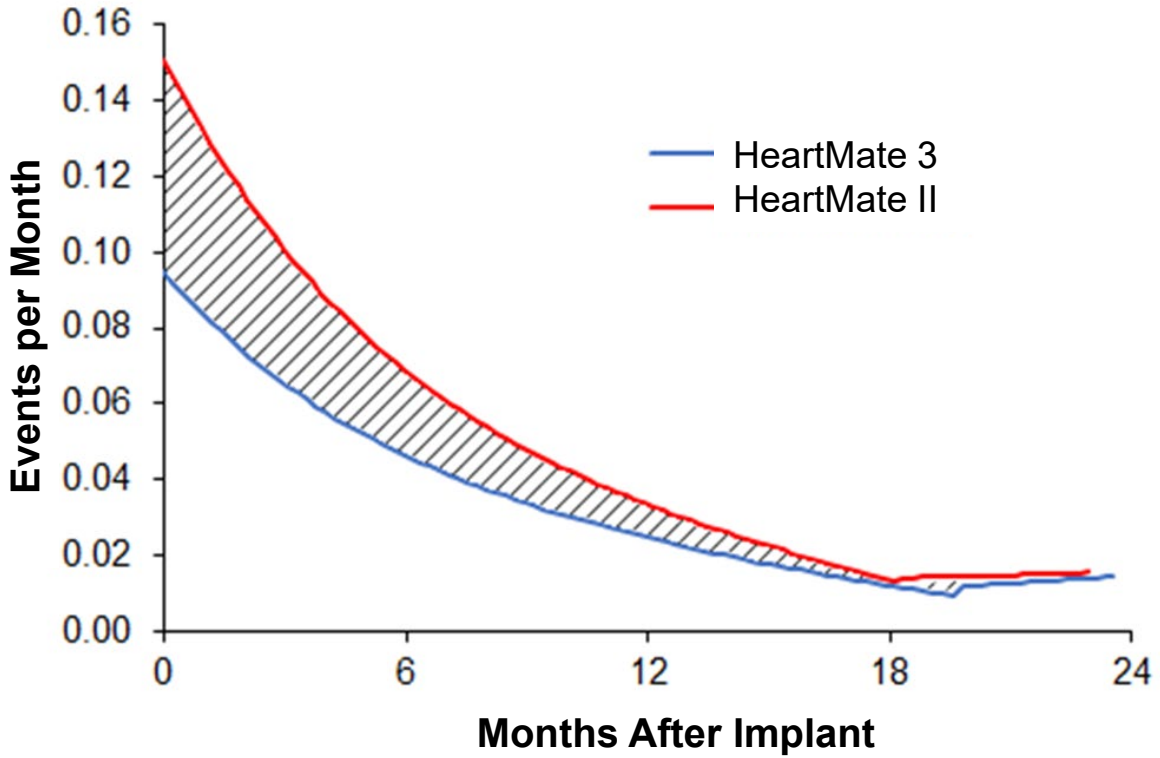
HR denotes hazard ratio; CI, confidence interval

Stroke and Bleeding Hazard Functions

Hazard Function for All Stroke



Hazard Function for All Bleed

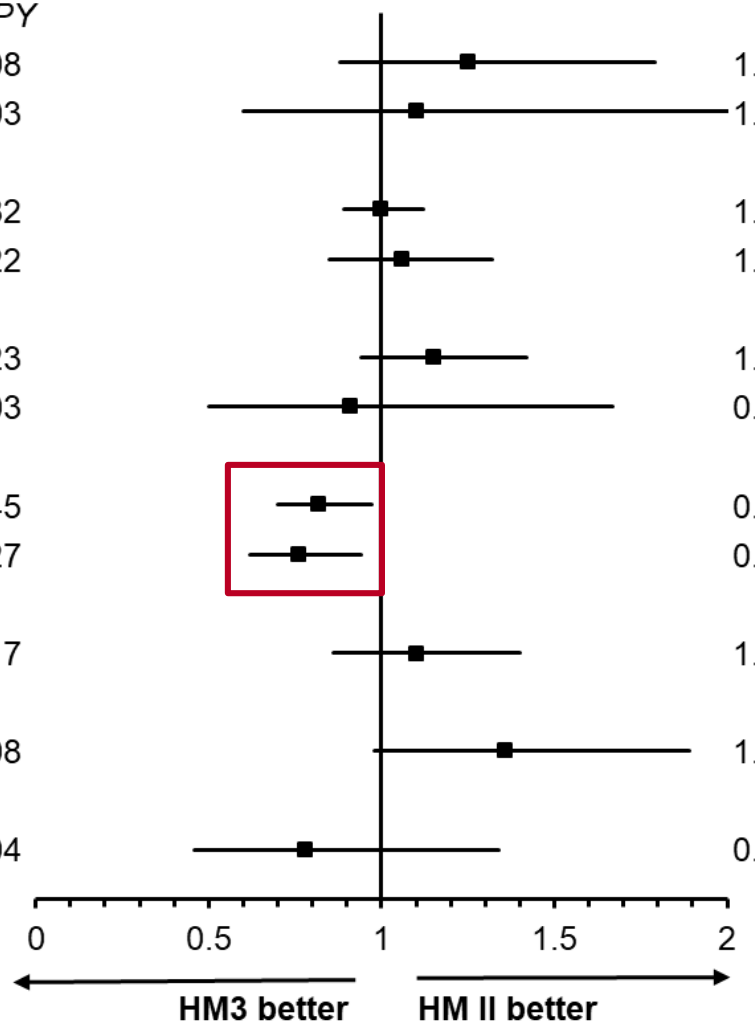


Mean arterial blood pressure, aspirin usage, and INR did not differ between the treatment arms during the trial.

MOMENTUM 3

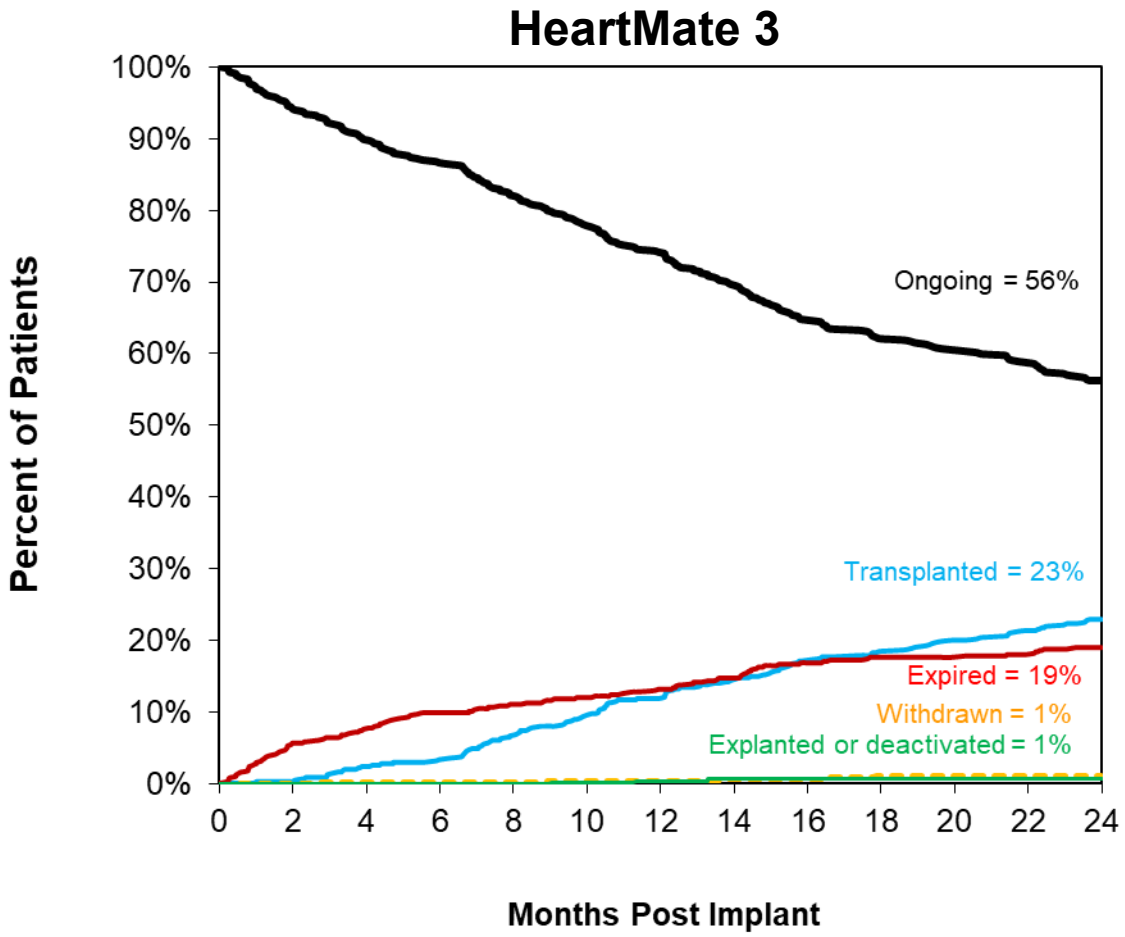
Other Adverse Events

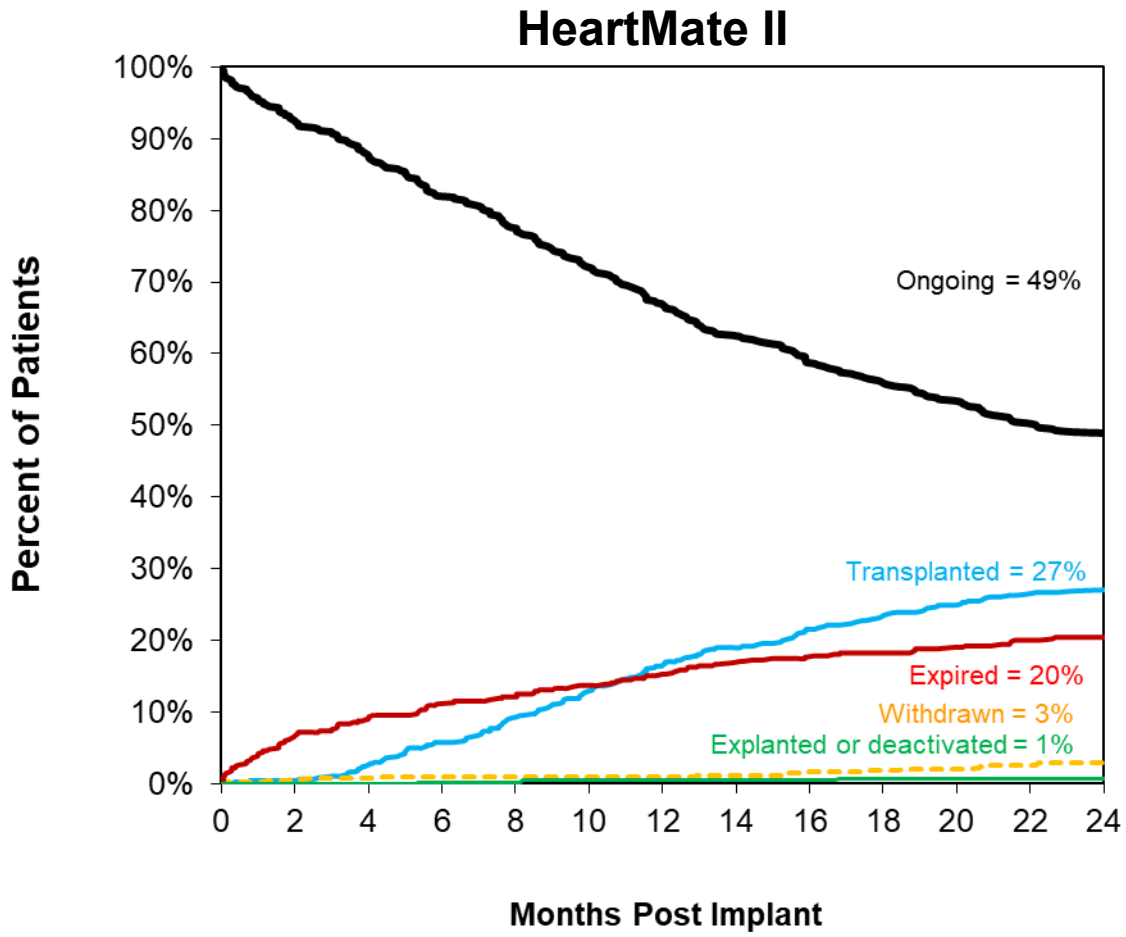
Adverse Event	HM3 *n (%)*	HM II *n (%)*	HM3 *EPPY*	HM II *EPPY*	Relative Risk (95% CI)	*P-Value**
Other neurologic event+	59 (11.5)	47 (9.3)	0.09	0.08	1.25 (0.88 - 1.79)	0.21
TIA	16 (3.1)	19 (3.8)	0.03	0.03	1.10 (0.60 - 2.02)	0.75
Any major infection	300 (58.3)	285 (56.4)	0.82	0.82	1.00 (0.89 - 1.12)	0.96
LVAS driveline infection	120 (23.3)	98 (19.4)	0.23	0.22	1.06 (0.85 - 1.32)	0.60
Any right heart failure	176 (34.2)	143 (28.3)	0.27	0.23	1.15 (0.94 - 1.42)	0.18
Managed with RVAS	21 (4.1)	21 (4.2)	0.03	0.03	0.91 (0.50 - 1.67)	0.76
Cardiac arrhythmia	185 (35.9)	207 (41.0)	0.37	0.45	0.82 (0.70 - 0.97)	0.02
Ventricular arrhythmia	107 (20.8)	128 (25.3)	0.20	0.27	0.76 (0.62 - 0.94)	0.01
Respiratory failure	111 (21.6)	98 (19.4)	0.19	0.17	1.10 (0.86 - 1.40)	0.44
Renal dysfunction	73 (14.2)	56 (11.1)	0.11	0.08	1.36 (0.98 - 1.89)	0.07
Hepatic dysfunction	25 (4.9)	27 (5.3)	0.03	0.04	0.78 (0.46 - 1.34)	0.38



HM3 denotes HeartMate 3; HMII HeartMate II; EPPY events per patient year; CI, confidence interval; TIA transient ischemic attack.
*P values were calculated with Poisson Regression. +Includes TIA, encephalopathy, seizure and neurologic events other than stroke

Competing Outcomes





Actuarial overall survival at 2-years was not significantly different between the groups:
79.0% for HeartMate 3 versus 76.7% for HeartMate II (log-rank P = 0.37)

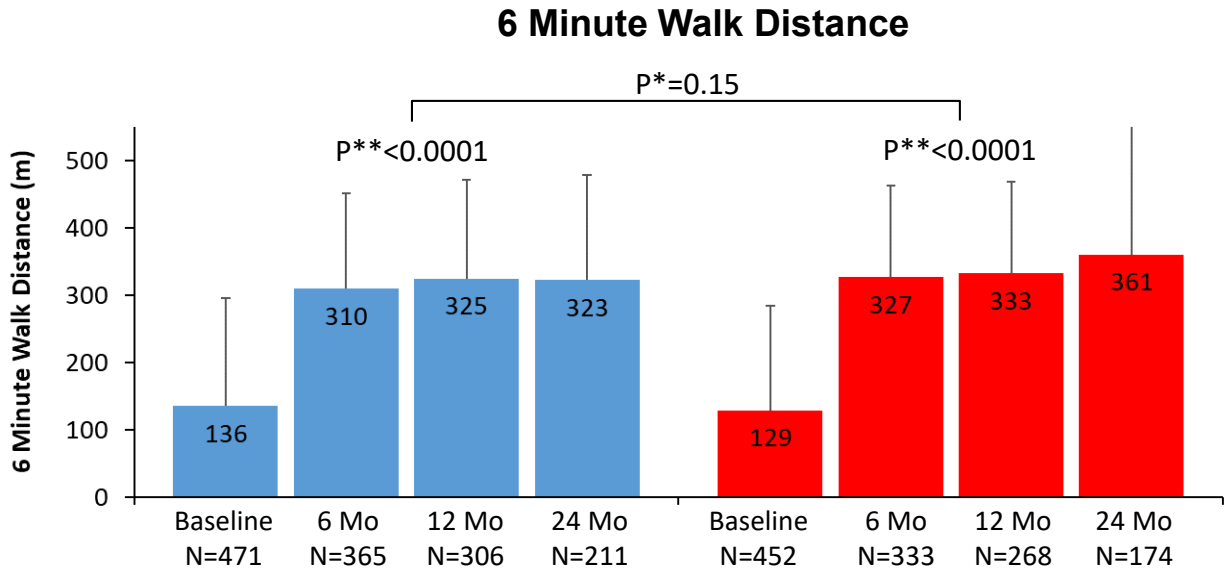
MOMENTUM 3

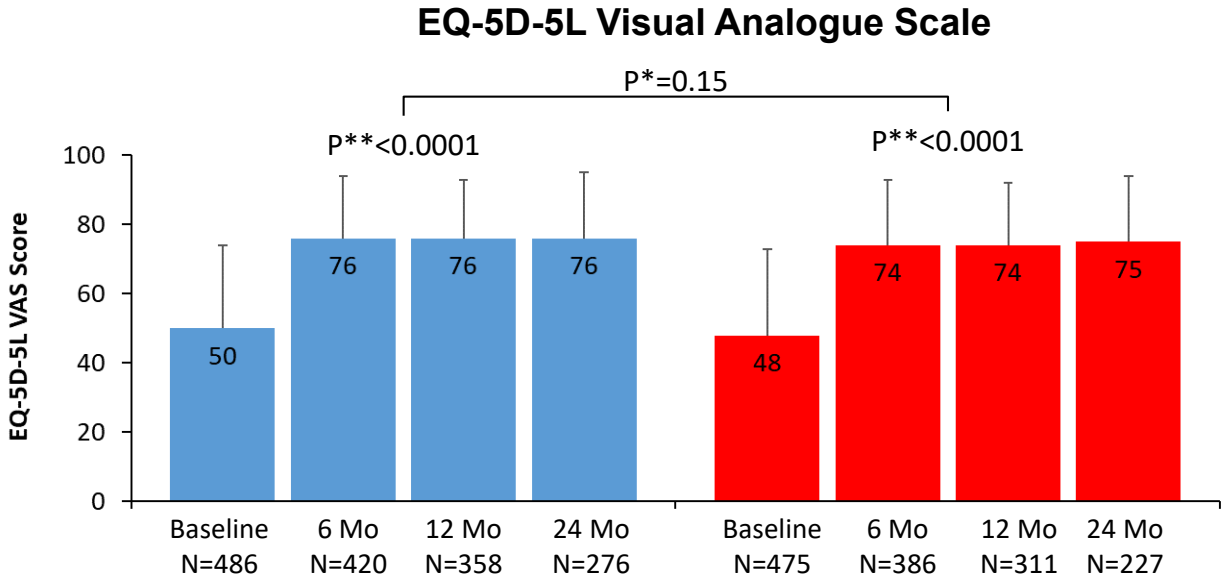
Hospitalization Profiles, Days Out of the Hospital and Readmissions

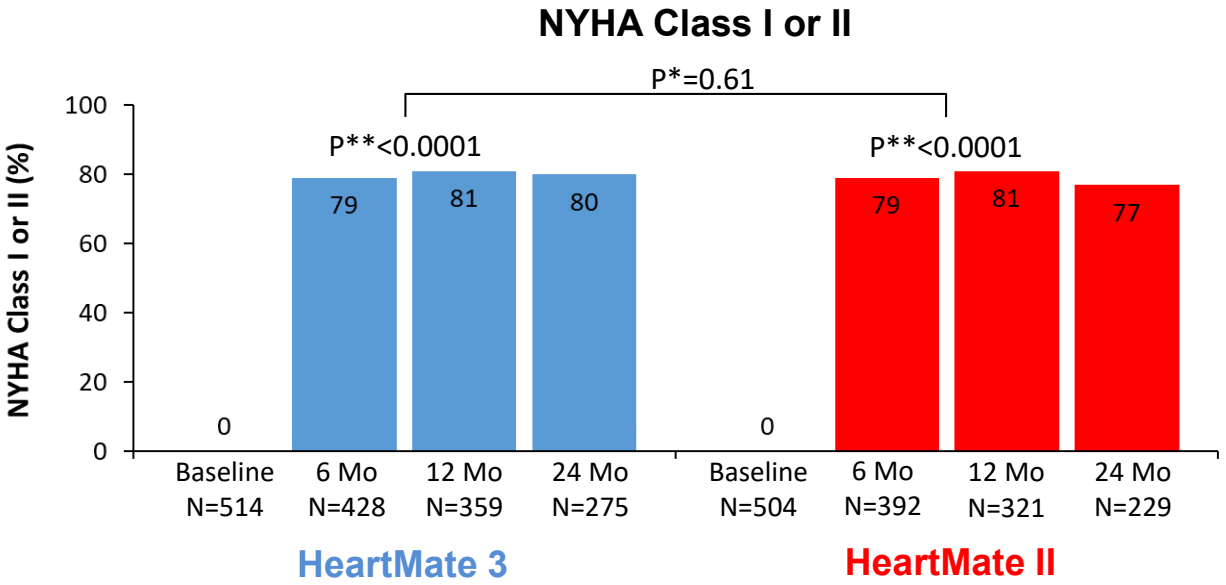
Patients Discharged on LVAD Support	HeartMate 3 (N=485)	HeartMate II (N=471)	Difference or HR (95%CI)	P*
Implant Hospitalization				
Median length of stay [interquartile range] - days	19 [14 to 25]	17 [14 to 24]	2 (0.7 to 3.3)	0.11
Post-Discharge				
Median duration of rehospitalization [interquartile range] - days	13 [4 to 37]	18 [6 to 40]	-5 (-8.7 to -1.3)	0.02
Median duration on LVAD support ***outside*** of hospital [interquartile range] - days	653 [333 to 696]	605 [259 to 690]	48 (-0.8 to 96.8)	0.008
Rate of rehospitalization for any cause - EPPY	2.26	2.47	0.92 (0.86 to 0.99)⁺	0.03

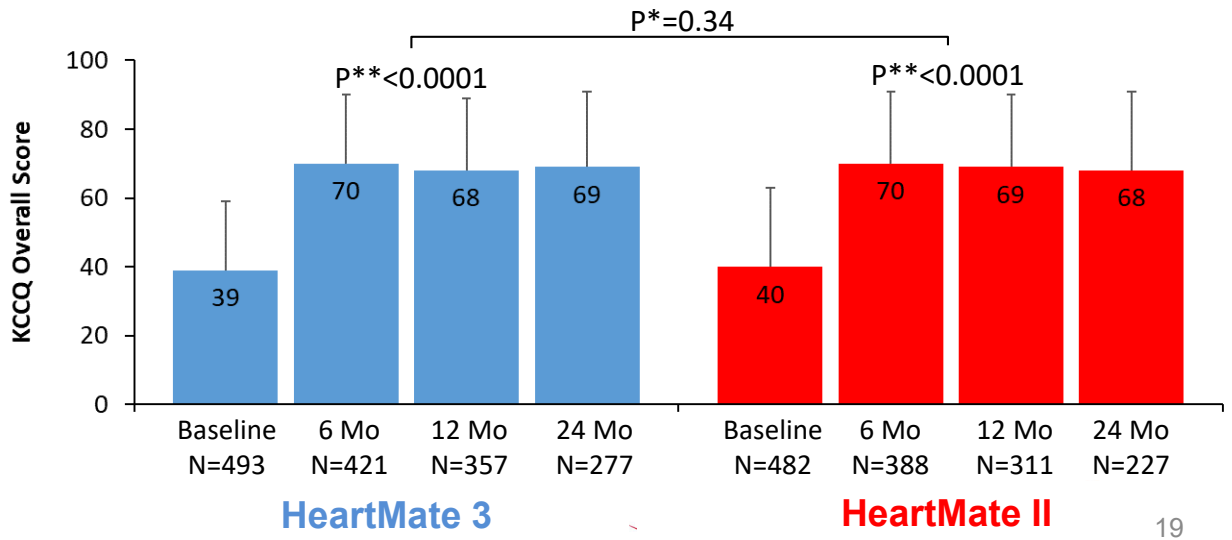
EPPY denotes events per patient year; HR, hazard ratio; CI, confidence interval.
*P values for differences in duration are from Wilcoxon Rank Sum test. ⁺HR was calculated from the Andersen-Gill model.

Functional Status and Quality of Life



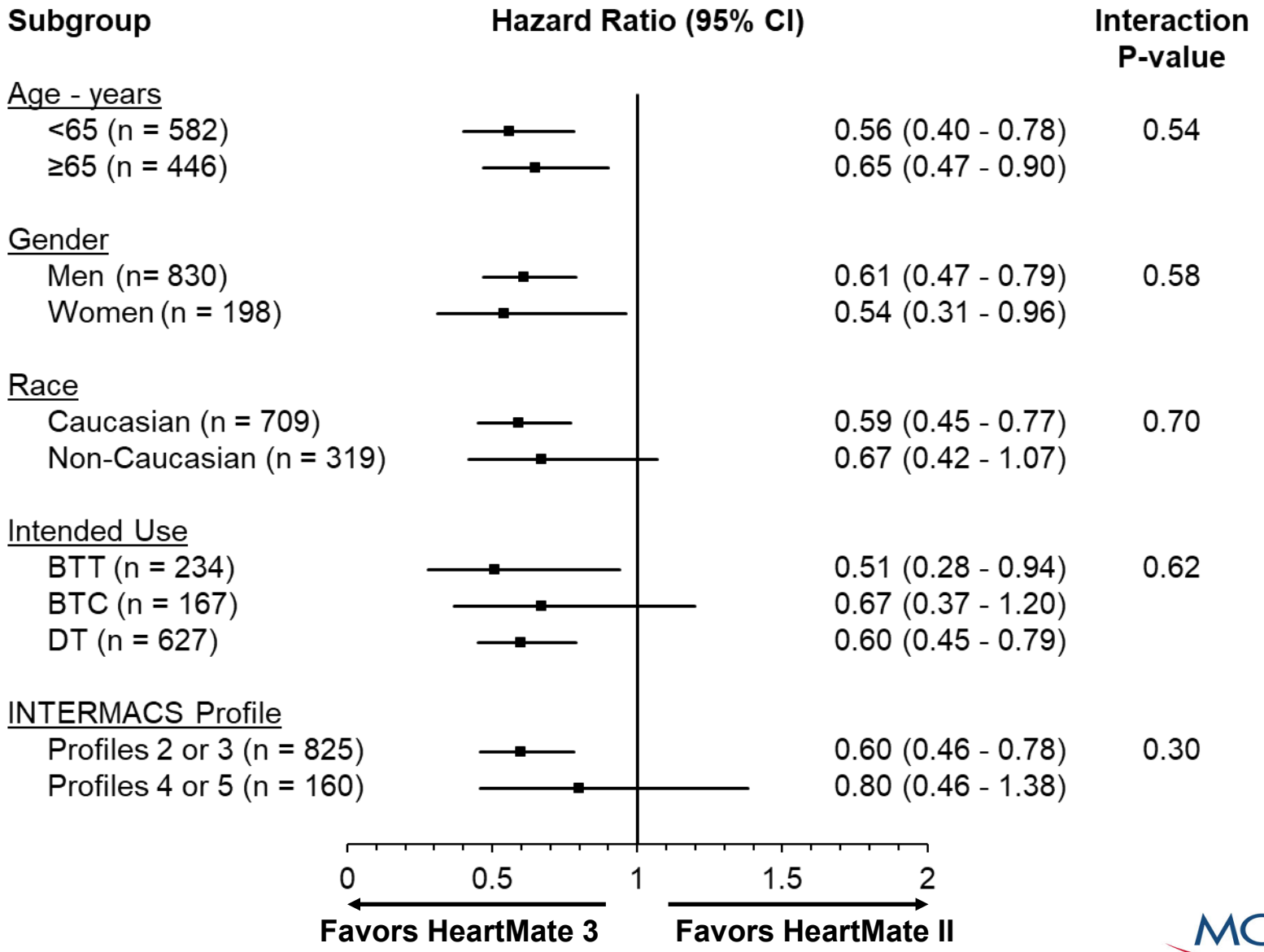






*P-value between treatment arms over time. **P-value for treatment over time. Longitudinal changes were analyzed with linear mixed-effects models using data from baseline, 3, 6, 12, 18, and 24 month visits.

Subgroup Analyses of the Primary Endpoint (ITT)

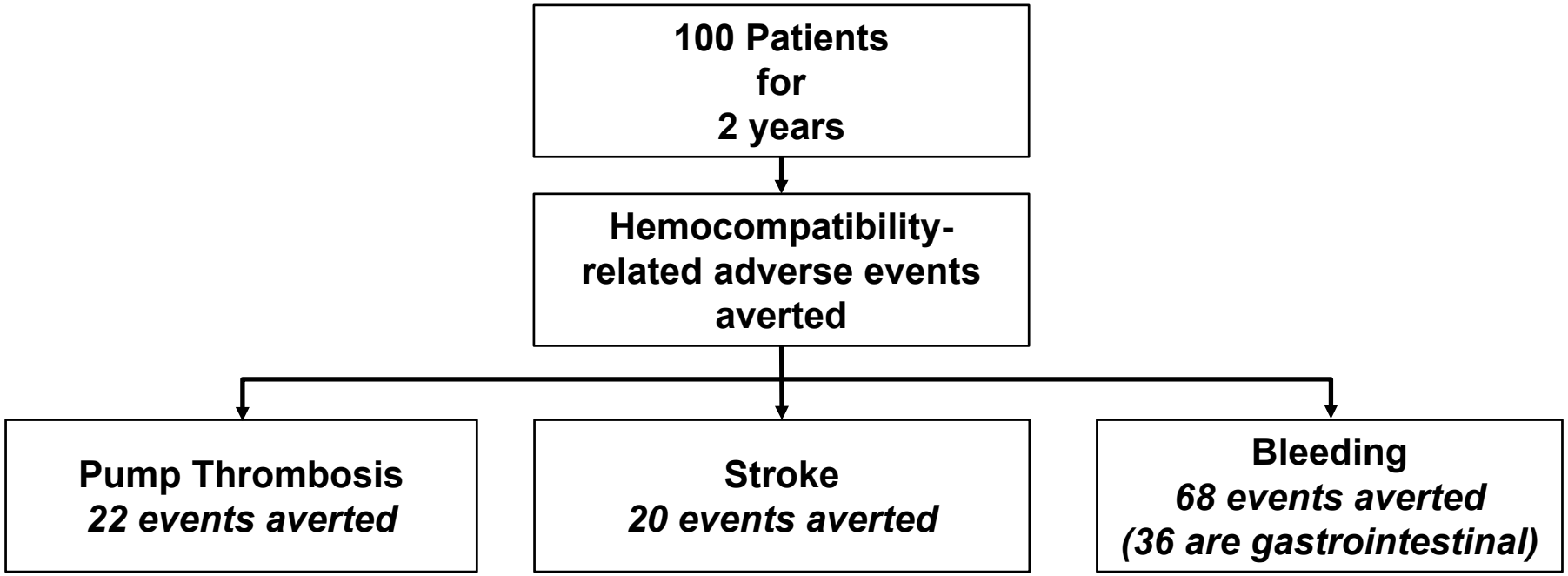


MOMENTUM 3

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

Net Clinical Benefit in the Trial

- The Number Needed to Treat over two years to avert at least 1 hemocompatibility-related adverse event (pump thrombosis, stroke, or bleed) is less than 1
- For every 100 patients implanted with HeartMate 3 rather than HeartMate II over a two-year period



Summary: A More Forgiving Pump

- In the largest LVAD study performed, the centrifugal-flow HeartMate 3 LVAS has demonstrated superior performance compared to the axial-flow HeartMate II pump with respect to:
  - Reduction in Pump Thrombosis
  - Reduction in Strokes of ***any type*** and of ***any severity***
  - Reduction in any Bleeding, particularly **gastrointestinal** bleeds
  - Reduction in Cardiac Arrhythmias, particularly ventricular arrhythmias
  - Reduction in readmissions and days spent in the hospital

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Fully Magnetically Levitated Left Ventricular Assist Device — Final Report

M.R. Mehra, N. Uriel, Y. Naka, J.C. Cleveland, Jr., M. Yuzefpolskaya, C.T. Salerno, M.N. Walsh, C.A. Milano, C.B. Patel, S.W. Hutchins, J. Ransom, G.A. Ewald, A. Itoh, N.Y. Raval, S.C. Silvestry, R. Cogswell, R. John, A. Bhimaraj, B.A. Bruckner, B.D. Lowes, J.Y. Um, V. Jeevanandam, G. Sayer, A.A. Mangi, E.J. Molina, F. Sheikh, K. Aaronson, F.D. Pagani, W.G. Cotts, A.J. Tatooles, A. Babu, D. Chomsky, J.N. Katz, P.B. Tessmann, D. Dean, A. Krishnamoorthy, J. Chuang, I. Topuria, P. Sood, and D.J. Goldstein, for the MOMENTUM 3 Investigators*

Available now on www.nejm.org

Links to all prior publications and presentations from the MOMENTUM 3 trial are available at **www.MOMENTUM3investigators.com**

MOMENTUM 3

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