# Comprehensive Analysis of Stroke in the Long-Term Cohort of the MOMENTUM 3 Study

## A Randomized Controlled Trial of the HeartMate 3 and HeartMate II Cardiac Pump

**Paolo C. Colombo, MD**, Mandeep R. Mehra, MD, Daniel J. Goldstein, MD, Jerry D. Estep, MD, Christopher Salerno, MD, Ulrich P. Jorde, MD, Jennifer A. Cowger, MD, Joseph C. Cleveland, Jr., MD, Nir Uriel, MD, Gabriel Sayer, MD, Eric R. Skipper, MD, Francis X. Downey, MD, Masahiro Ono, MD, PhD, Robert Hooker, Jr, MD, Anelechi C. Anyanwu, MD, Michael M. Givertz, MD, Claudius Mahr, DO, Ia Topuria, MPH, Sami I. Somo, PhD, Daniel L. Crandall, PhD, Douglas A. Horstmanshof, MD

MOMENTUM 3

ClinicalTrials.gov: NCT02224755

# Relevant Financial Relationship Disclosure Statement

***Clinical Outcomes by Intended Goal of Therapy in the MOMENTUM 3 Clinical Trial: Analysis of the Full Cohort***

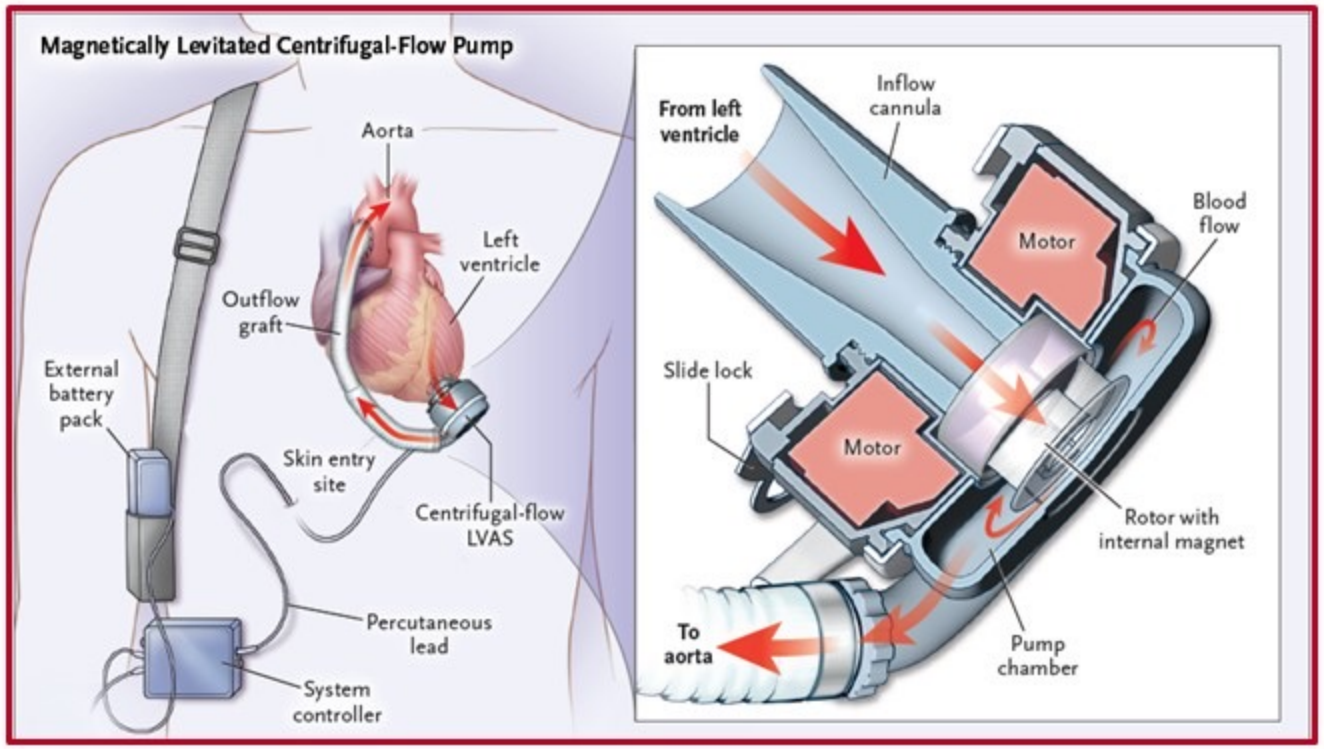
## Presenter: Daniel Goldstein, MD

**I WILL NOT discuss off label use and/or investigational use of drugs/devices**

**The following relevant financial relationships exist related to this presentation:**

| | |
|---|---|
| *D. Goldstein* | *Educator and Surgical Proctor, Consultant – Abbott, National Principal Investigator - NIH-VEST Trial, Consultant -Terumo Inc.* |
| *M. Mehra* | *Consultant (paid to B&W Hospital) - Abbott, Consultant - Portola, Bayer, Xogenex, Steering Committee - Medtronic, Janssen, DSMB - Mesoblast, Scientific Advisory Board - NupulseCV, FineHeart* |
| *N. Uriel* | *Consultant - Abbott, Medtronic* |
| *J. Cleveland* | *Consultant - Abbott* |

# 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 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

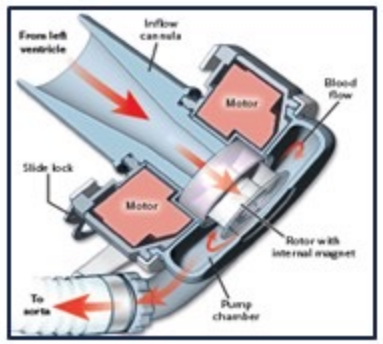
# MOMENTUM 3 Trial

- MOMENTUM 3 is a randomized controlled trial of the HM3 centrifugal-flow pump versus the HMII axial-flow pump in patients with advanced heart failure, irrespective of intended goal of support (bridge-to-transplantation or destination therapy)
- **Key exclusion criteria** included planned biventricular support, irreversible end-organ dysfunction, or active infection



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.

# MOMENTUM 3 - Study Design




Patient meets MOMENTUM 3 eligibility criteria?

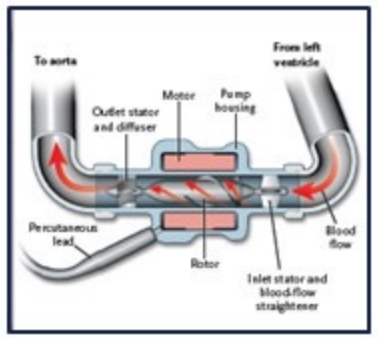
Randomization 1:1

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

Additional 72 patients enrolled

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

Full Cohort
N=1028
*2-year follow-up*



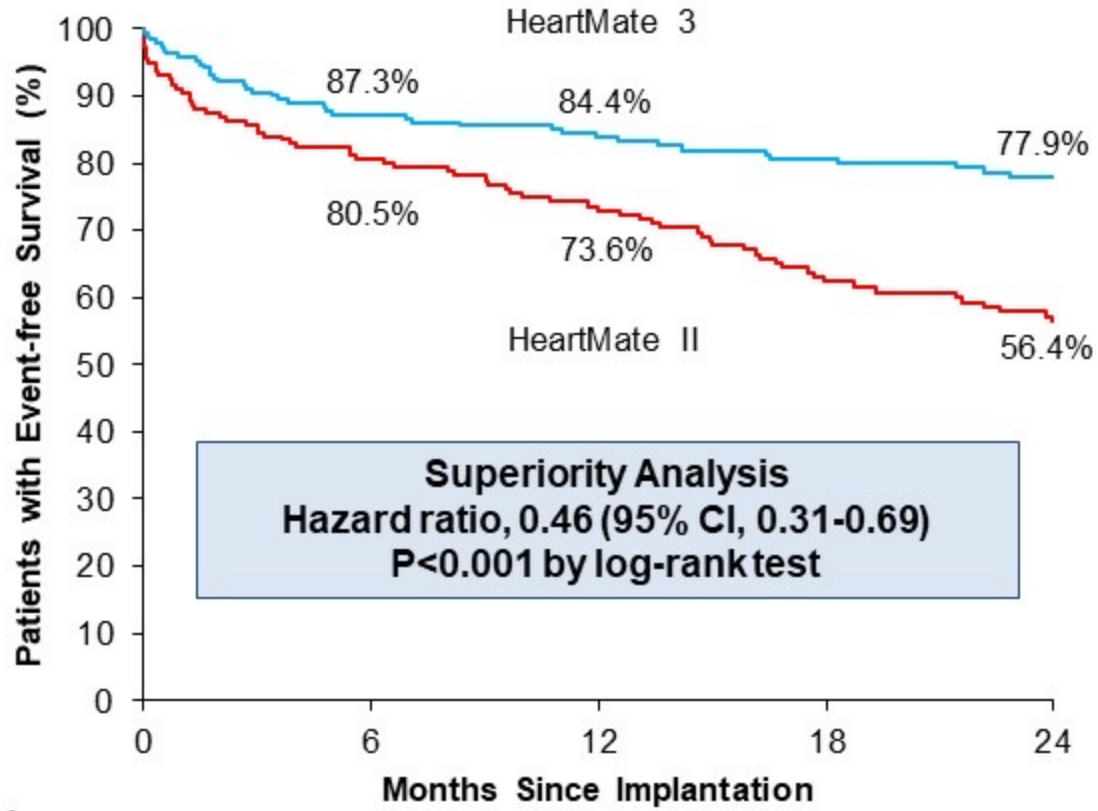

MOMENTUM 3



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

# Long Term Cohort (N=366) - Primary End Point Analysis (ITT)

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



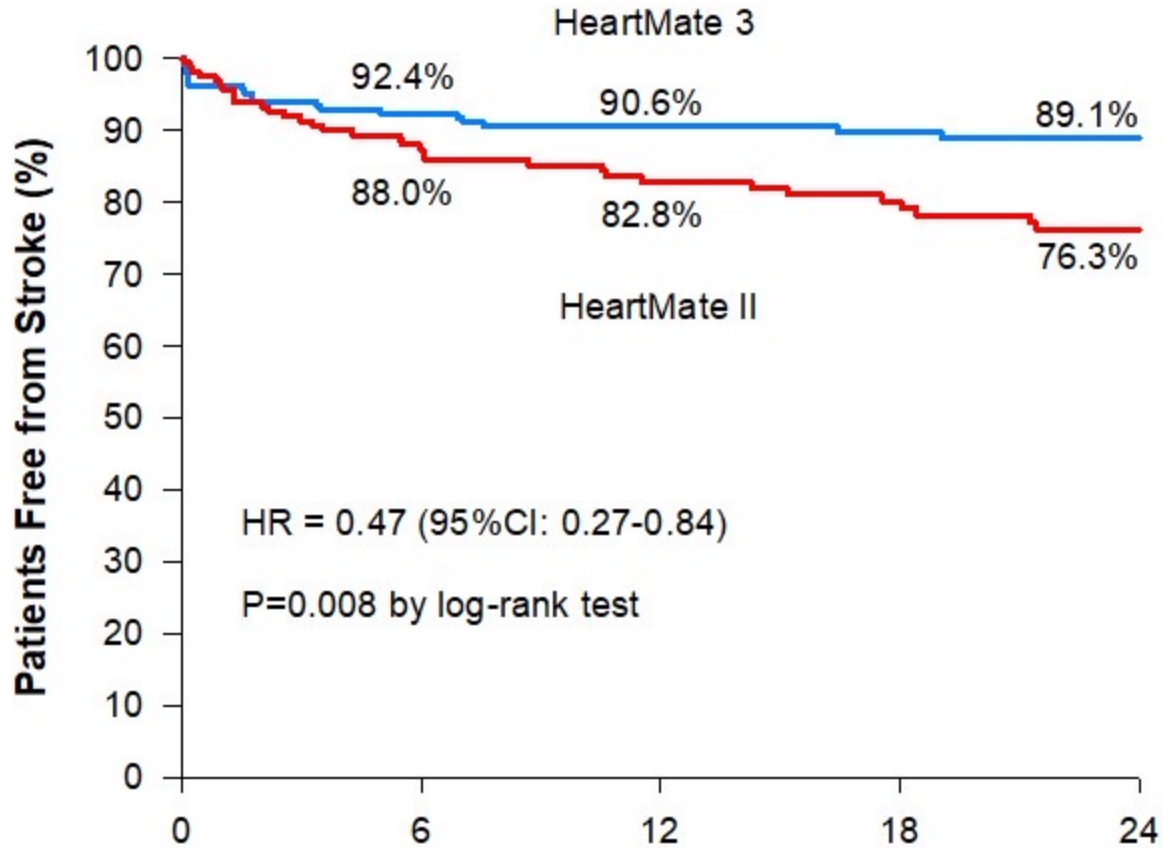

| No. at Risk | | | | | |
|---|---|---|---|---|---|
| HeartMate 3 | 190 | 161 | 141 | 122 | 111 |
| HeartMate II | 176 | 134 | 114 | 90 | 75 |

mRS denotes modified Rankin Score; CI, confidence interval



Mehra et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *N Engl J Med* 2018;378:1386-1395.

# Key Adverse Events
## *Stroke*




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

MOMENTUM 3



HR denotes hazard ratio; CI, confidence interval

Mehra et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. *N Engl J Med* 2018;378:1386-1395.

# Study Objectives

1. To evaluate the patterns and provide a time-dependent comparison of stroke events in HM3 vs. HMII patients over 2-years

2. To conduct an exploratory analysis of clinical predictors of stroke events

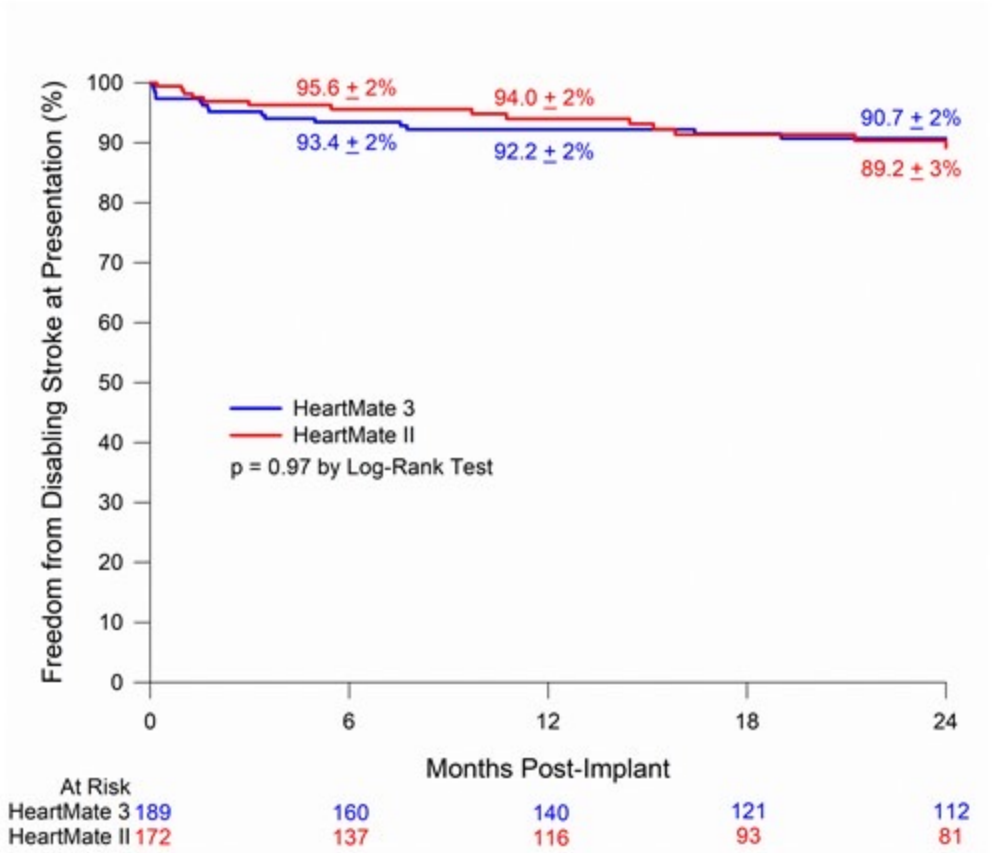
3. To assess clinical outcome of strokes by
   - Starting with the **first event and initial presentation**
   - Comparing the **subtypes** (ischemic stroke (IS) vs. hemorrhagic stroke (HS))
   - Evaluating the **severity of neurologic deficit** (disabling, modified Rankin Scale (mRS)>3 vs. non-disabling, mRS≤3)

# Results

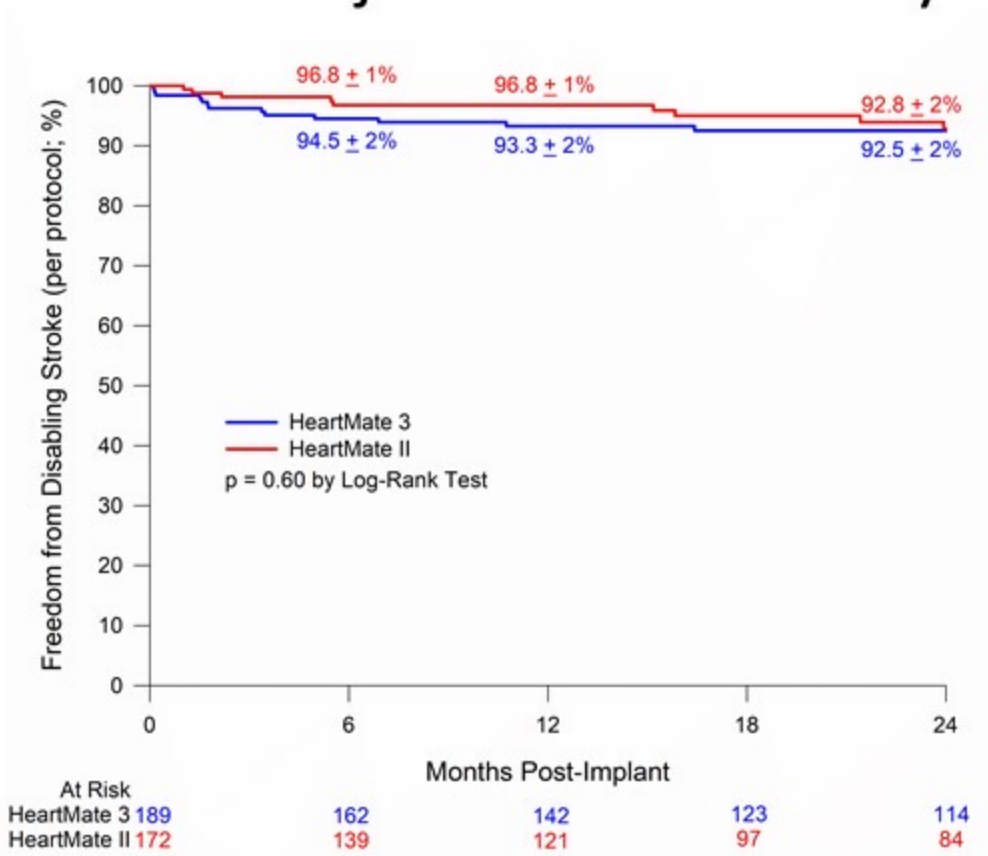
| | HeartMate 3 (n = 189) | | | HeartMate II (n = 172) | | |
|---|---|---|---|---|---|---|
| | EPPY | Patients (%) | Events | EPPY | Patients (%) | Events |
| **Stroke Events** | 0.08 | 19 (10.1) | 22 | 0.18 | 33 (19.2) | 43 |
| | | | | | | |
| **Stroke by Subtype** | | | | | | |
| Hemorrhagic Stroke | 0.03 | 8 (4.2) | 8 | 0.07 | 16 (9.3) | 17 |
| Ischemic Stroke | 0.05 | 12 (6.3) | 14 | 0.11 | 23 (13.4) | 26 |

# Disabling Stroke

## At Initial Presentation



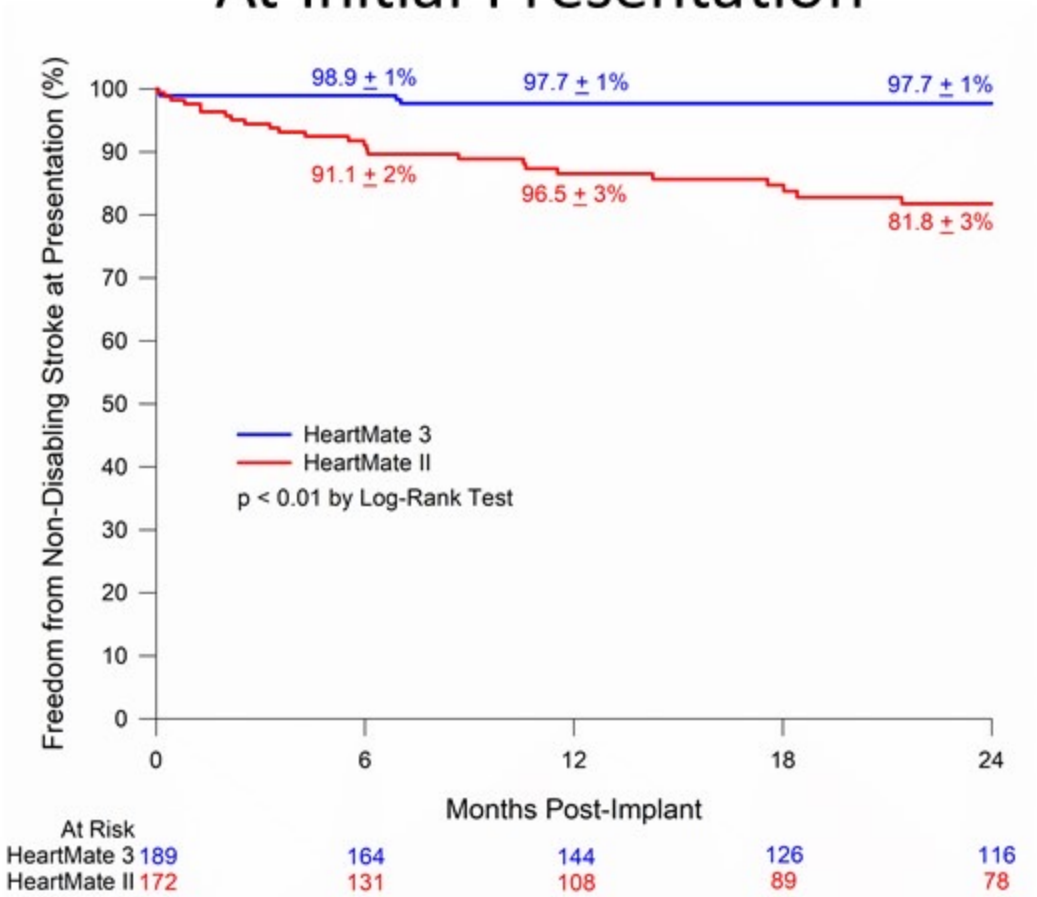

## mRS Adjudicated at 60-Days



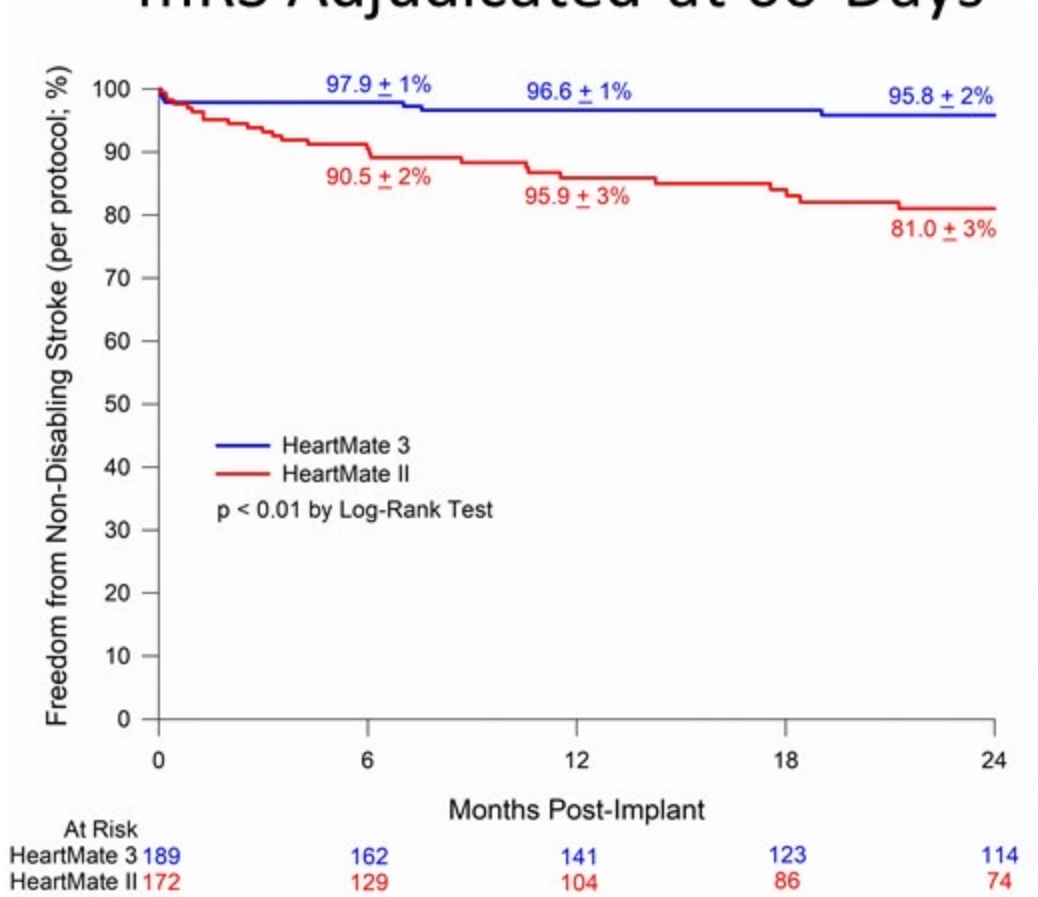

MOMENTUM 3

# Non-Disabling Stroke

## At Initial Presentation




## mRS Adjudicated at 60-Days

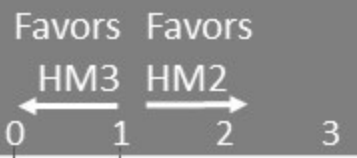


| Baseline Characteristics | HeartMate 3 (n = 189) | | | HeartMate II (n = 172) | | |
|---|---|---|---|---|---|---|
| | No Stroke | Stroke | p-value | No Stroke | Stroke | p-value |
| | n=170 | n=19 | | n=139 | n=33 | |
| **Age - years** | 60 ± 12 | 67 ± 8 | 0.001 | 59 ± 13 | 60 ± 9 | 0.53 |
| **Gender (Male)** | 135 (79%) | 14 (74%) | 0.56* | 115 (83%) | 25 (76%) | 0.35 |
| **Destination Therapy** | 100 (59%) | 11 (58%) | 0.94 | 87 (63%) | 19 (58%) | 0.59 |
| **BSA - $m^2$** | 2.1 ± 0.3 | 2.0 ± 0.2 | 0.05 | 2.0 ± 0.3 | 2.1 ± 0.2 | 0.61 |
| **BMI - $kg/m^2$** | 29.3 ± 6.3 | 26.7 ± 5.2 | 0.09 | 28.1 ± 5.9 | 29.4 ± 5.3 | 0.23 |
| **Ischemic Etiology** | 72 (42%) | 8 (42%) | 0.98 | 67 (48%) | 17 (52%) | 0.73 |
| **Baseline Blood Pressure – mmHg** | | | | | | |
| **MAP** | 81 ± 11 | 82 ± 10 | 0.63 | 78 ± 10 | 80 ± 10 | 0.48 |
| **Systolic** | 110 ± 16 | 109 ± 12 | 0.81 | 105 ± 13 | 111 ± 14 | 0.04 |
| **Diastolic** | 67 ± 11 | 70 ± 10 | 0.19 | 66 ± 11 | 65 ± 11 | 0.85 |
| **INTERMACS profile** | | | 0.30* | | | 0.77 |
| **1-2-3** | 148 (87%) | 15 (79%) | | 115 (83%) | 28 (85%) | |
| **4-5** | 22 (13%) | 4 (21%) | | 24 (17%) | 5 (15%) | |
| **Medical History** | | | | | | |
| **Atrial Fibrillation** | 70 (41%) | 11 (58%) | 0.16 | 69 (50%) | 12 (36%) | 0.17 |
| **Diabetic** | 44 (26%) | 2 (11%) | 0.17* | 22 (16%) | 6 (18%) | 0.74 |
| **Stroke or TIA** | 26 (15%) | 6 (32%) | 0.10* | 19 (14%) | 9 (27%) | 0.06 |
| **Hypertension (requiring medication)** | 114 (67%) | 12 (63%) | 0.73 | 91 (65%) | 24 (73%) | 0.43 |
| **Known PFO** | 10 (6%) | 2 (11%) | 0.34* | 18 (13%) | 1 (3%) | 0.13* |
| **Carotid Artery Disease** | 92 (54%) | 10 (53%) | 0.90 | 70 (50%) | 23 (70%) | 0.045 |
| **Creatinine - mg/dl** | 1.4 ± 0.4 | 1.4 ± 0.4 | 0.95 | 1.3 ± 0.4 | 1.4 ± 0.3 | 0.21 |
| **BUN - mmol/l** | 28 ± 14 | 31 ± 18 | 0.36 | 26 ± 12 | 30 ± 12 | 0.13 |
| **Bilirubin - mg/dl** | 1.0 ± 0.5 | 1.2 ± 0.6 | 0.09 | 1.1 ± 0.5 | 1.0 ± 0.5 | 0.41 |

BMI – Body Mass Index; BSA – Body Surface Area; LVEF – Left Ventricular Ejection Fraction; PFO – patent foramen ovale; TIA – Transient Ischemic Attack.
*Fishers Exact Test; †Includes Asian, Native Hawaiian or Pacific Islanders, and Others

# Stroke Rates Across the Duration of Support

| Time (Days) | Stroke Events (Pts/Patients on-going, %) | | Events per patient-year | | Odds Ratio (HM3 vs HMII) OR (95% CI) |
|---|---|---|---|---|---|
| | HM3 | HMII | HM3 | HMII | |
| Overall (0-733 Days) | 22 (19/189, 10%) | 43 (33/172, 19%) | 0.08 | 0.18 | 0.47 (0.26 - 0.86), p=0.01 |
| - Perioperative (0-30 Days) | 7 (7/189, 3.7%) | 6 (6/172,3.5 %) | 0.46 | 0.44 | 1.06 (0.35 - 3.23), p=0.91 |
| - Short-term (31-180 Days) | 7 (7/182, 3.8%) | 16 (13/161, 8.1%) | 0.10 | 0.26 | 0.46 (0.18 - 1.17), p=0.09 |
| - Long-term (181-730 Days) | 8 (5/165, 3.0%) | 21 (17/141, 12.1%) | 0.04 | 0.13 | 0.23 (0.08 - 0.63), p=0.01 |



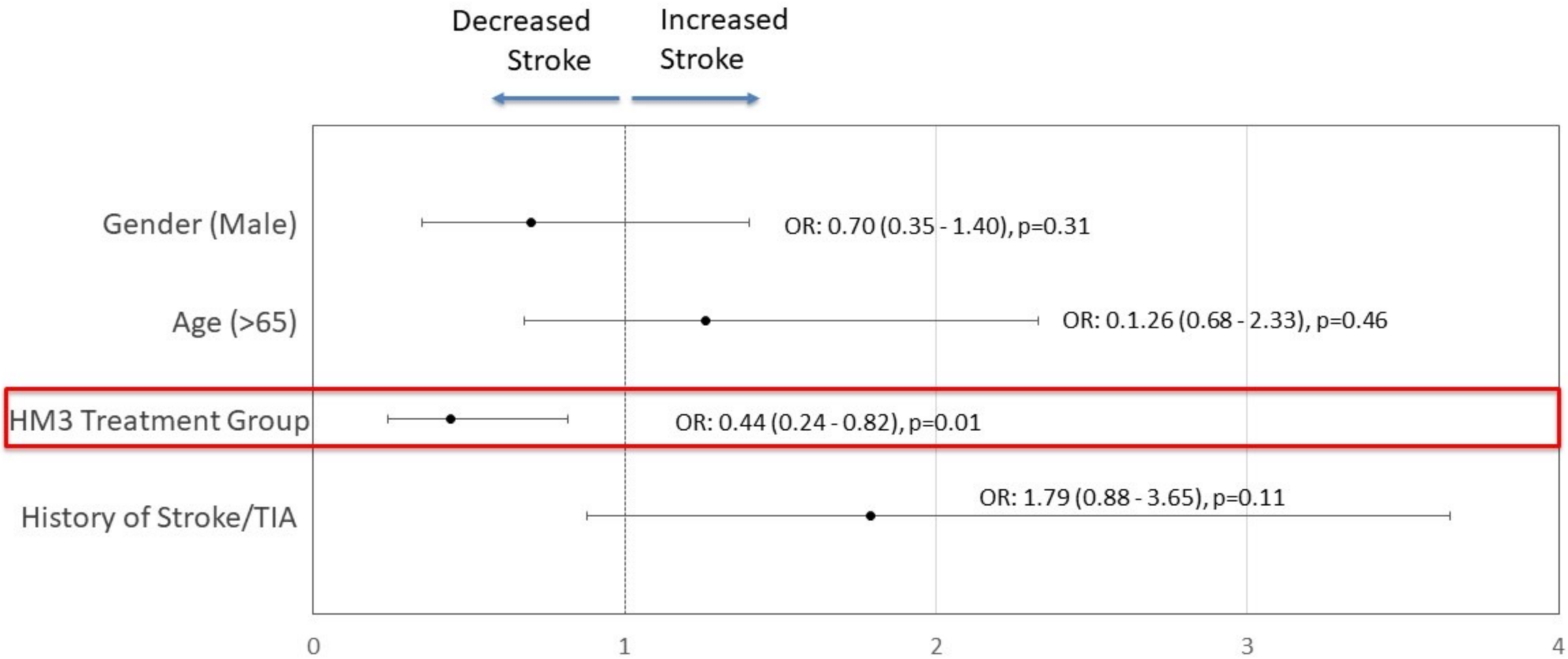

MOMENTUM 3

# Univariable Modeling – Stroke vs. No Stroke

| Variable | Stroke (n=52) | No Stroke (n=309) | p-Value |
|---|---|---|---|
| Gender (Male) | 39/52 (75%) | 250/309 (81%) | 0.33 |
| Age (>65) | 22/52 (42%) | 119/309 (39%) | 0.60 |
| Destination Therapy | 30/52 (58%) | 187/309 (61%) | 0.70 |
| Randomization (HM3 Arm) | 19/52 (37%) | 139/309 (45%) | 0.02 |
| History of Stroke or TIA | 13/52 (25%) | 49/309 (16%) | 0.11 |
| Atrial Fibrillation | 23/52 (44%) | 139/309 (45%) | 0.92 |
| Left Atrial Appendage Closure | 3/52 (6%) | 24/309 (8%) | 0.61 |
| Mean Arterial Pressure at Discharge* | 83.2 ± 11.2 (37) | 80.4 ± 9.1 (288) | 0.09 |
| Mean Arterial Pressure (>95 mmHg, baseline preop) | 5/51 (10%) | 26/309 (8%) | 0.74 |
| Gastrointestinal Bleeding† | 11/52 (21%) | 78/309 (25%) | 0.53 |
| Infection† | 26/52 (50%) | 165/309 (53%) | 0.65 |
| Suspected Pump Thrombosis† | 5/52 (10%) | 19/309 (6%) | 0.36 |
| Aspirin at 30 Days§ | 30/39 (77%) | 265/309 (86%) | 0.15 |
| INR at 30 Days§ | 2.2 ± 0.7(39) | 2.3 ± 0.8 (296) | 0.51 |

*Excludes strokes occurring pre-discharge †For the stroke group only adverse events (GI Bleeding, Infection, and Suspected Pump Thrombosis) that occurred prior to the first stroke were included. Prior to stroke only – exclude any events occurring after last stroke event (include if it is between stroke events because it could have influenced the next stroke). §Excludes patients with strokes prior to 30 Days.

# Multivariable model



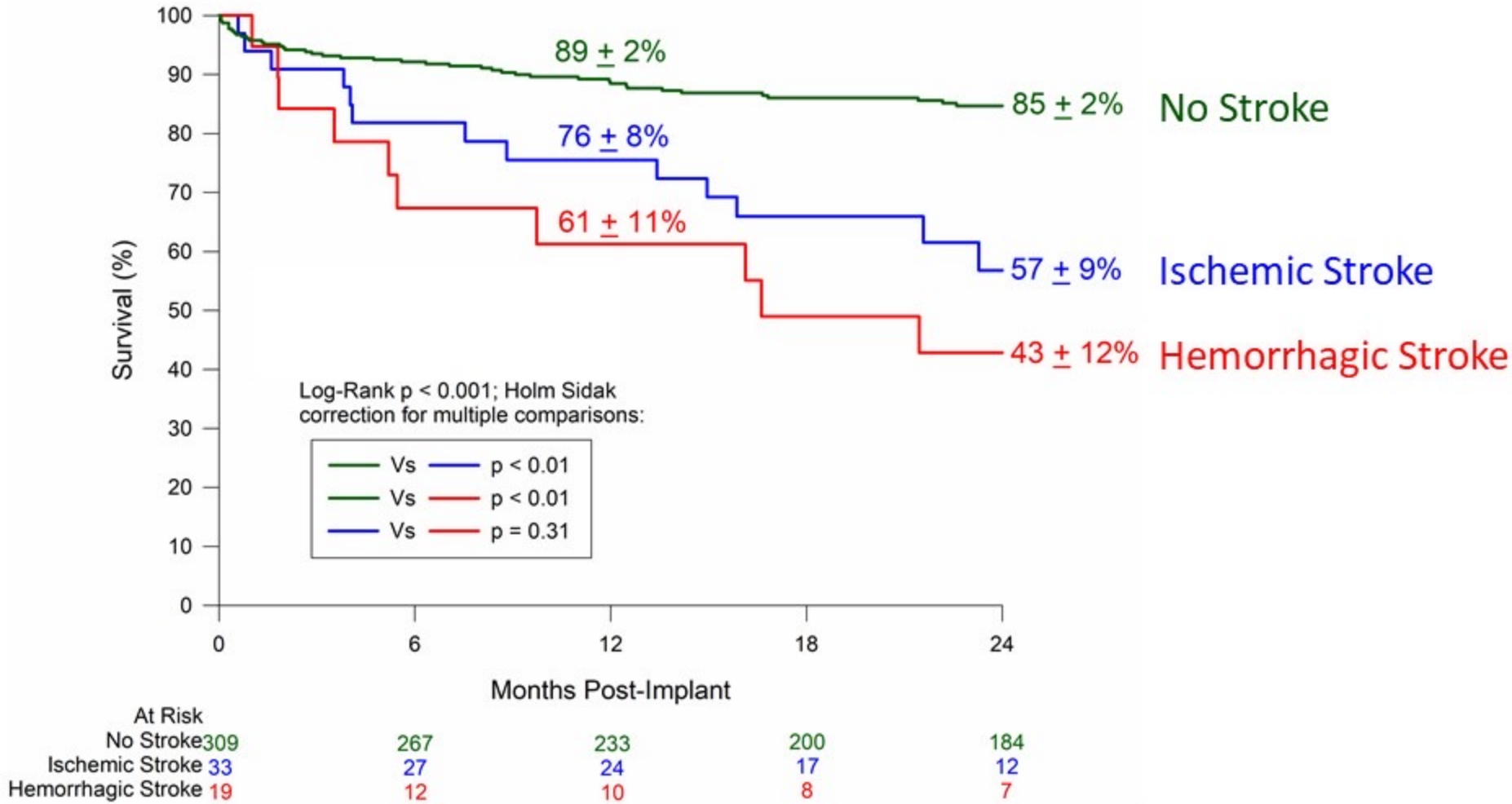
# Adjudicated Causes of Death in Stroke Patients

| | Deaths n=23/52 (44%) | Days Post-Implant | Days Post-Stroke |
|---|---|---|---|
| **Neurologic** | | | |
| - Ischemic Stroke | 2/23 (9%) | 24, 125 | 20, 22 |
| - Hemorrhagic Stroke | 11/23 (48%) | 167 [31-656]* | 1 [0-62]* |
| **Non-Neurologic** | | | |
| - Right Heart Failure | 3/23 (13%) | 18, 123, 270 | 15, 84, 33 |
| - Infection | 3/23 (13%) | 458, 494, 713 | 327, 165, 204 |
| - Bleeding | 2/23 (9%) | 108, 661 | 2, 478 |
| - Pump Thrombosis | 1/23 (4%) | 411 | 303 |
| - Respiratory Failure | 1/23 (4%) | 117 | 114 |

*Median [Range]

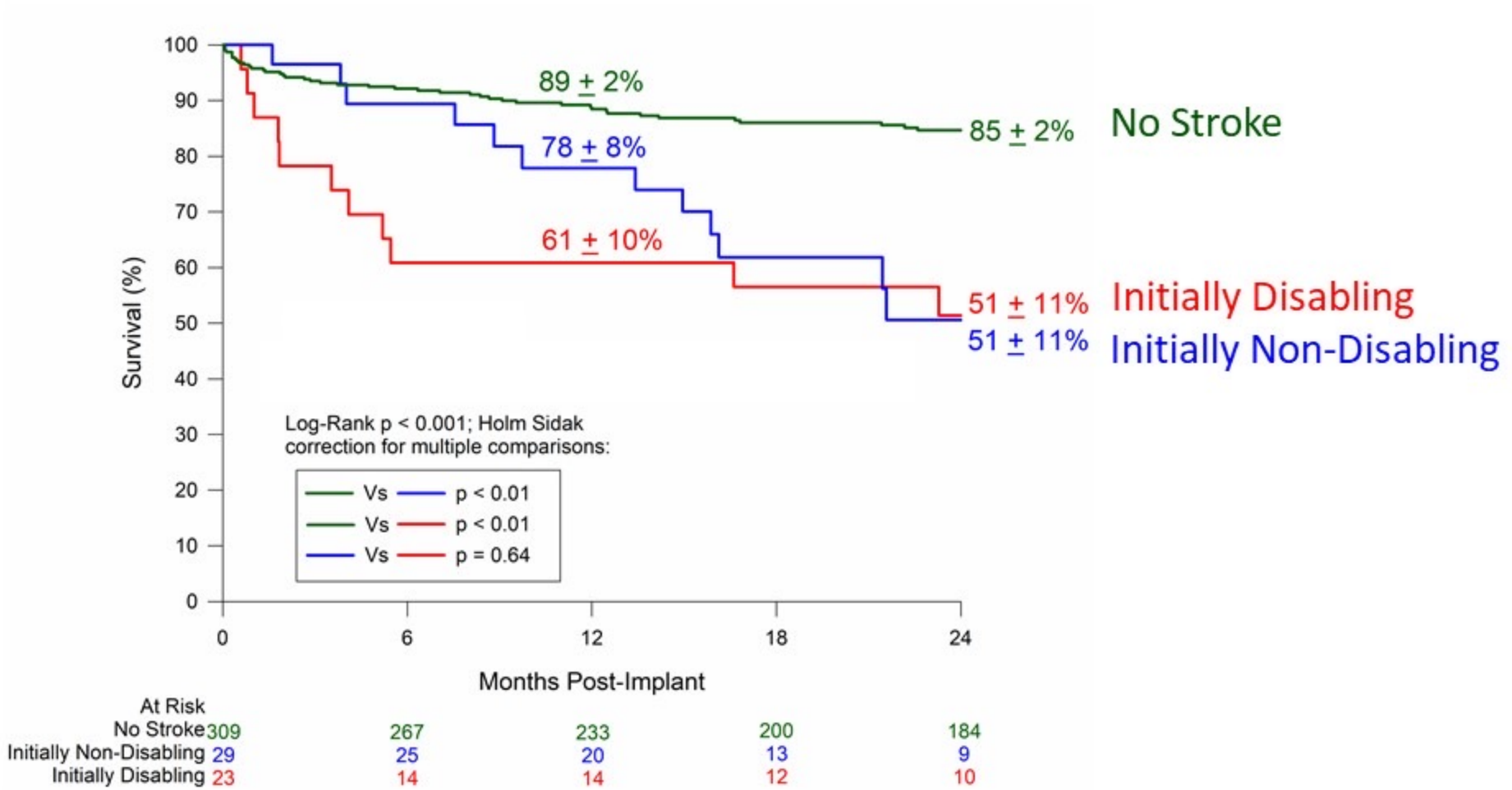
MOMENTUM 3

# Survival Post-Implant by Subtype: Ischemic vs. Hemorrhagic



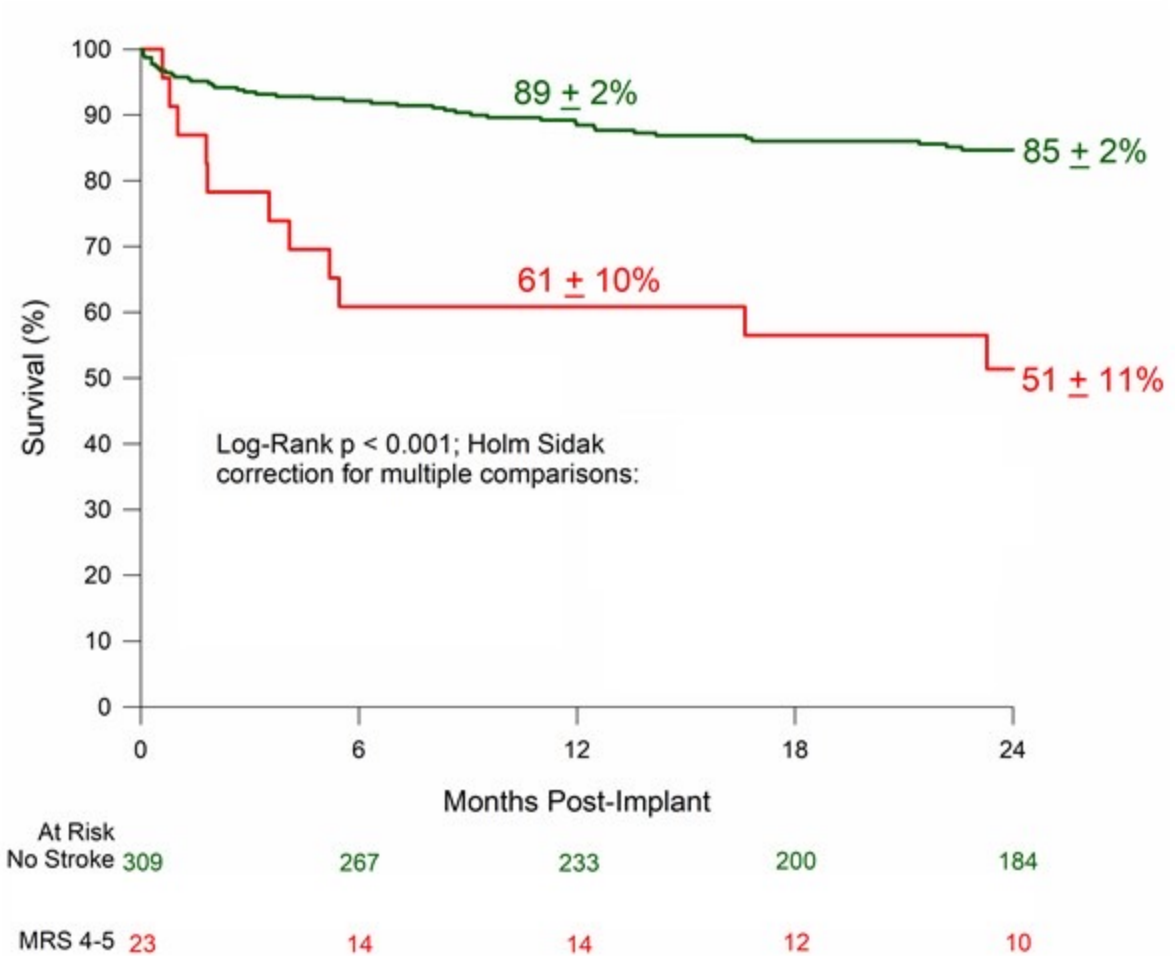

MOMENTUM 3

# Survival Post-Implant - Disabling vs. Non-Disabling




MOMENTUM 3

# Survival Post-Implant - Disabling vs. Non-Disabling

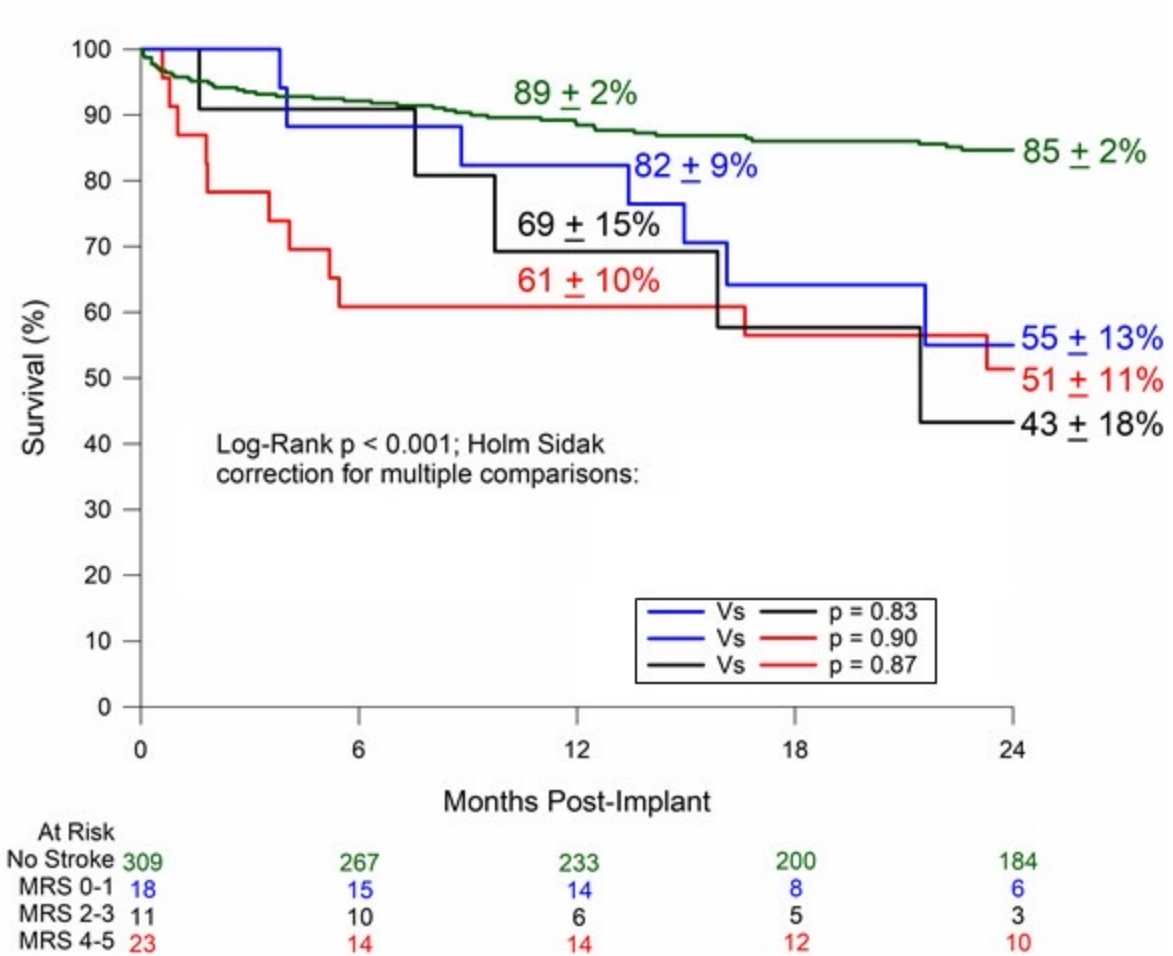



No Stroke

Initially Disabling
Stroke mRS 4-5

MOMENTUM 3

# Survival Post-Implant - Disabling vs. Non-Disabling




No Stroke

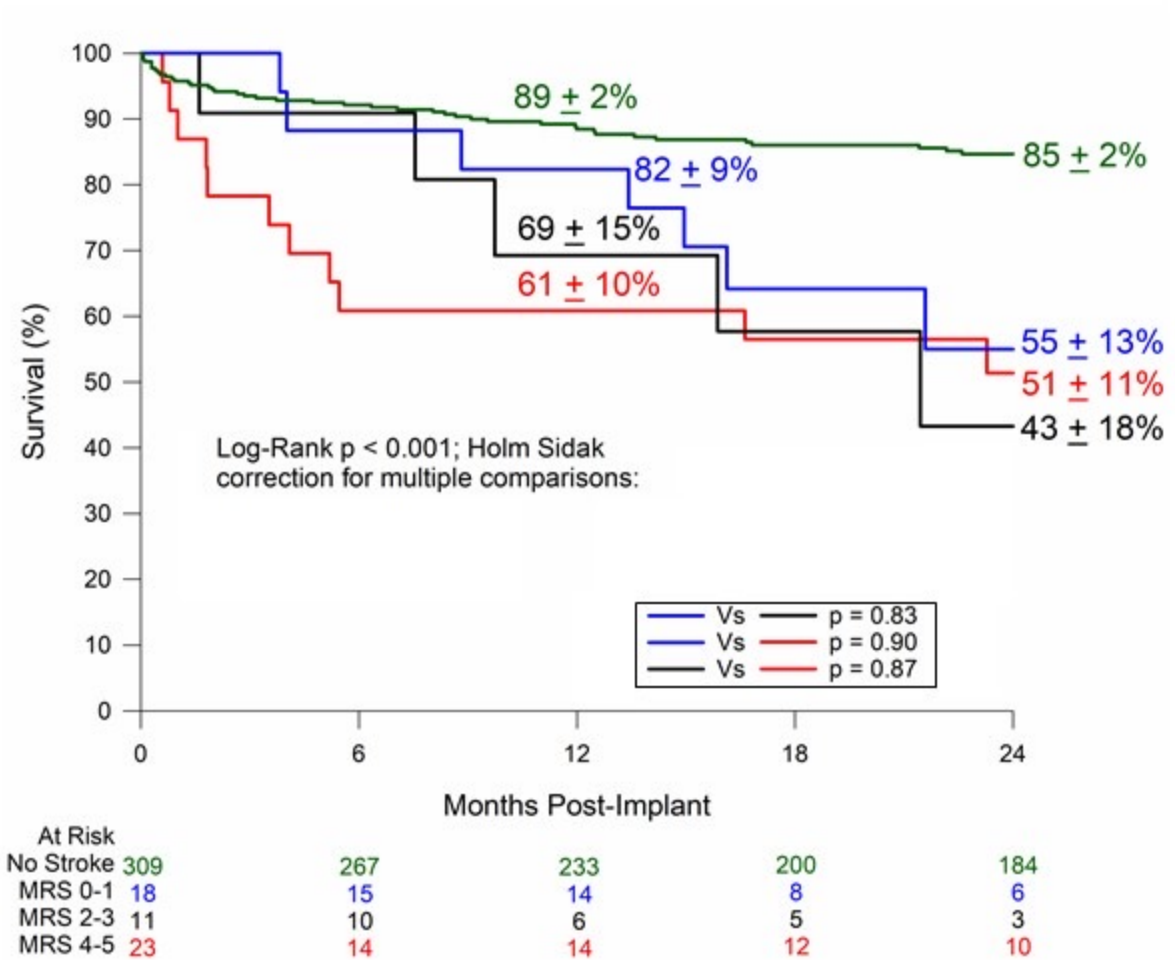
Stroke mRS 0-1

Initially Disabling Stroke mRS 4-5

Stroke mRS 2-3

MOMENTUM 3

# Survival Post-Implant - Disabling vs. Non-Disabling




No Stroke

Stroke mRS 0-1

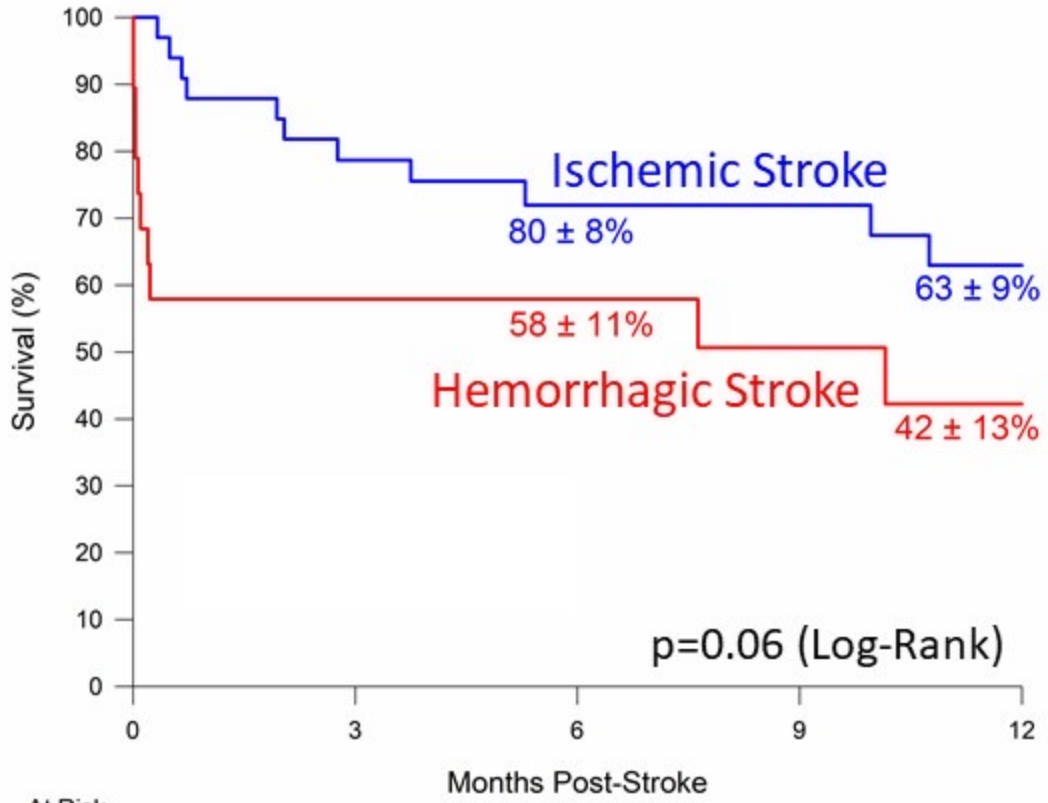
Initially Disabling Stroke mRS 4-5

Stroke mRS 2-3

MOMENTUM 3

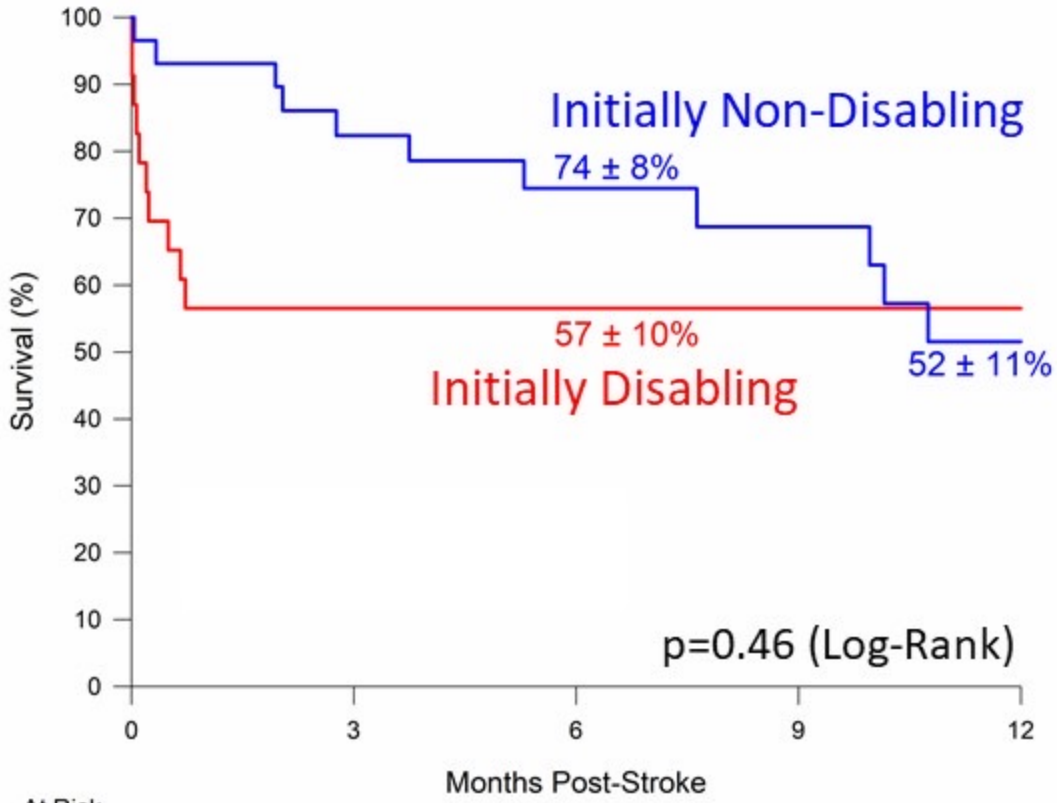
# Survival Post-Stroke

## Subtype




| At Risk | | | | | |
|---|---|---|---|---|---|
| Ischemic Stroke | 33 | 25 | 20 | 16 | 14 |
| HemorrhagicStroke | 19 | 9 | 9 | 6 | 5 |

## Severity




| At Risk | | | | | |
|---|---|---|---|---|---|
| Initially Non-Disabling | 29 | 22 | 18 | 12 | 9 |
| Initially Disabling | 23 | 12 | 11 | 10 | 10 |

MOMENTUM 3

# Treatments of Stroke (excludes multiple strokes)

| Treatment | Patients |
|---|---|
| **Ischemic** | **n=20** |
| Anticoagulation/Antiplatelet Intensification | 11 (55%) |
| Anticoagulation/Antiplatelet Continuation | 7 (35%) |
| Intra-arterial Embolectomy | 0 (0%) |
| Other* | 2 (10%) |
| **Ischemic with Hemorrhagic Component/Conversion** | **n=5** |
| Anticoagulation/Antiplatelet Hold | 5 (100%) |
| **Hemorrhagic** | **n=16** |
| Anticoagulation/Antiplatelet Hold | 5 (31%) |
| Anticoagulation/Antiplatelet Reversal† | 6 (38%) |
| Surgical† | 3 (19%) |
| None | 4 (25%) |
| *One patient treated with FFP due to INR > 7. †Two patients treated with both anticoagulation reversal and surgery | |

# Conclusions

- The use of the HeartMate 3 magnetically levitated LVAD in patients with advanced heart failure lowers stroke rates when compared with the axial flow HeartMate II pump
- Clinical trials of LVAD therapy must not selectively report functionally disabling stroke rates; rather they must primarily consider overall stroke rates due to the similar prognostic implications of either non-disabling or disabling strokes
- We also highlight the importance of the need to develop aggressive treatment algorithms for stroke events, specific to LVAD therapy in an effort to reduce subsequent disability and mortality


**Simultaneously Published online at http://circ.ahajournals.org**

THANK YOU to MOMENTUM 3 INVESTIGATORS, LVAD COORDINATORS and The HEART TEAM

***DISCLOSURES*: THE MOMENTUM 3 TRIAL IS SPONSORED BY ABBOTT**



MOMENTUM 3

**Abbott**
6101 Stoneridge Dr., Pleasanton, CA 94588 USA, Tel: 1 925 847 8600
Cardiovascular.Abbott/HeartMate3

**Rx Only**
**Brief Summary:** Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

**HeartMate 3™ LVAS Indications:** The HeartMate 3™ Left Ventricular Assist System is indicated for providing short- and long-term mechanical circulatory support (e.g., as bridge to transplant or myocardial recovery, or destination therapy) in adult and pediatric patients with advanced refractory left ventricular heart failure and with an appropriate body surface area.

**HeartMate 3™ LVAS Contraindications:** The HeartMate 3 Left Ventricular Assist System is contraindicated for patients who cannot tolerate, or who are allergic to, anticoagulation therapy.

**HeartMate 3™ LVAS Adverse Events:** Adverse events that may be associated with the use of the HeartMate 3 Left Ventricular Assist System are: death, bleeding, cardiac arrhythmia, localized infection, right heart failure, respiratory failure, device malfunctions, driveline infection, renal dysfunction, sepsis, stroke, other neurological event (not stroke-related), hepatic dysfunction, psychiatric episode, venous thromboembolism, hypertension, arterial non-central nervous system (CNS) thromboembolism, pericardial fluid collection, pump pocket or pseudo pocket infection, myocardial infarction, wound dehiscence, hemolysis (not associated with suspected device thrombosis) or pump thrombosis.



MOMENTUM 3